SAJOUS'S
ANALYTIC CYCLOPEDIA
OF
PRACTICAL MEDICINE

BY
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ASSISTED BY
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WITH THE ACTIVE CO-OPERATION OF OVER
ONE HUNDRED ASSOCIATE EDITORS

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PREFACE
TO THE NINTH EDITION

THE preceding edition, as stated in its preface, incorporated the new lines of thought opened up, modified or indirectly influenced by the war. This applied not only to surgery as generally believed, but also practically to every disease to which the human male is heir, including various tropical disorders brought to the seat of active operations by troops and laborers from Asia, Africa, etc., where such diseases prevailed. The aftermath of this great aggregate of clinical observations engendered a period of intensive study calculated to establish on a solid footing the deductions hastily vouchsafed. The present, or ninth edition, even though issued but two years after its predecessor, has for its purpose to present what suggestive data of this character have been recorded during this brief period. While the majority of subjects reviewed in the work have been more or less added to or altered, some have required considerable readjustment, those of Fractures and Dislocations for instance, which have been brought up to date by Professor W. Wayne Babcock who, as Lieutenant-Colonel and Chief Surgeon of one of the greatest of our military hospitals during the war, treated an enormous number of injuries of all sorts.

It was also suggested in the previous edition that as much of the material incorporated therein might ultimately have to be modified through elucidative inquiry carried on after the excitement accompanying or immediately following strife had been allayed, the newer data presented at the time had been introduced in small type, the larger type text being intended only to portray those features of our knowledge which prolonged experience in practice had sanctioned. In the short space of two years, the data thus poised on a permanent foundation may be said to have been few, but wherever this seemed warranted, they were introduced in the large type text. In some

directions other than those connected with the war, as in the management of the disorders of parturition, the endocrinopathies, protein sensitization, protein therapy, adenoid vegetations, etc., greater latitude was afforded and taken advantage of.

The transitions in all branches of medicine are so numerous that the value of the present edition will be perpetuated by periodical supplements which, following up each clue in the eight volumes, will enable their readers to keep well abreast of the times without being obliged to purchase a new Cyclopedia.

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SAJOUS'S
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A

ABDOMEN, SURGERY OF.— Abdominal surgery in its wide sense includes a great variety of operative procedures which are based upon the same general principles as the ones which are included in this article, but which have been left to contributors in the other departments: all of the external hernias, a good part of renal surgery, the surgery of the abdominal walls, and all of the pelvic surgery of the female.

This article takes account of that part of abdominal surgery which includes hollow and solid viscera, the former comprising the various parts of the alimentary tube between the diaphragm and the brim of the pelvis, all biliary and pancreatic ducts and the gall-bladder. The solid viscera belonging to this series of articles comprise the liver, spleen and pancreas only.

There is a general sameness of the alimentary canal in these various parts which leads to more or less correspondence between operations done at the different levels of this tract. Operations of the biliary ducts and gall-bladder also have many points in common, and they resemble in a way the operative resources that are employed for the genitourinary passages.

We propose to consider the special features of abdominal surgery in two ways: first, as a series of typical operations which are intended to correct certain diseased states, and then from the other direction as a series of diseased states to be relieved by operative procedures of various kinds. It seems therefore of advantage to consider the typical operations for the stomach, small and large intestines and biliary passages as operations which are in a way applicable to all surgical conditions of these organs. Surgical diseases of the peritoneum, appendix, liver, spleen and pancreas require separate consideration in detail, because of the relative absence of typical operations, making the treatment more or less individualized for each case.

THE FOURTH ERA IN SURGERY.— In abdominal surgery we have perhaps the best field for object lessons relative to the new fourth or physiologic era in surgery. The first era in surgery was the heroic, under which practically no abdominal surgery was done. In the second or anatomic era of surgery, abdominal

operations were in general so danger-
ous that few were attempted, except-
ing in cases of great emergency, and
usually with a fatal ending. The
third or pathologic era of surgery was
based upon the studies of Pasteur and
of Lister. Aside from its technique
of preventing the development of bac-
teria in wounds, it included the idea
of removing all products of infection
with painstaking care.

Notwithstanding the injury that
was done to patients by surgeons
carrying out the principles of this era,
abdominal surgery made its first great
advances. Detailed attention was
given to the deliberate disposal of
products of infection found within the
peritoneal cavity, and little or no at-
tention was paid to the natural re-
sistance forces contained within the
patient himself. There was an enor-
mous waste of such forces, in fact, in
our abdominal surgery of the patho-
logic era.

The entirely modern or physiologic
era is based upon the studies of
Metchnikoff and Wright, and includes
the principal idea of allowing the
patient to retain his natural forces
in such a way as to gain control of
infections. Metchnikoff and his fol-
lowers taught us that certain cells of
the blood and lymph circulatory sys-
tems not only disposed of bacteria
daily under normal conditions, but
that these cells were increased in
number rapidly to meet emergen-
cies of infection. These investigators
showed also that bacteria were de-
stroyed by certain fixed body cells.
Wright and his followers showed fur-
ther that, in the presence of an infec-
tion, several kinds of antibodies were
elaborated in the animal economy,
and these antibodies lent their aid in

removing infections and in destroy-
ing certain toxins that were produced
by bacteria. The principles of this
fourth or physiologic era of surgery
brought us face to face with the
problem of operating in such a way
as to leave the patient in the very
best condition for managing infec-
tions himself with his own phagocytes
and antibodies, and led to a revolu-
tion in methods, forcing us to drop
out of our technique such parts of the
system of the third or pathologic era
as interfered with the ability of the
patient to produce phagocytes and
antibodies.

For instance, a prolonged and
painstaking operation for removing
all of the pus from the peritoneal
cavity so shocked the great vaso-
motor centers of the patient that they
were palsied, and unable promptly to
take up the work of conducting the
manufacture of phagocytes and anti-
bodies, with which the patient him-
self could dispose of the products of
infection much better than the sur-
geon could do it in his crude mechani-
cal way.

Unnecessarily prolonged operations
acted in precisely the same way;
and where we had thought best to
expend a half-hour in carrying out
the theories of the pathologic era in
surgery, we may now expend five
minutes under the principles of the
physiologic era.

Experimentation has shown that shock
is produced more readily by manipulation
of the abdominal viscera than by gross in-
juries, when animals are fully anesthetized,
especially when the anesthetic used is
chloroform. The parietal peritoneum and
mesenteries are especially sensitive. These
facts emphasized some years ago by Mum-
mery and Symes ar now fully recognized.
EDITORS.

A long period of anesthesia was commonly required for thorough work under the principles of the third era, but we now know, from our experiments upon animals, that individuals profoundly under the influence of alcohol, or of ether or of chloroform, temporarily lose resistance to infections, and some acute infections which would not gain headway under a few minutes of anesthesia may seize the opportunity to gain ascendancy if the anesthesia is prolonged for an hour or two. Bulky or complicated drainage apparatus, acting as a foreign body, further produces derangement of function of the vasomotors in such a way as to prevent the patient from manufacturing his phagocytes and antibodies. We are just entering, then, the era in which the greatest degree of success is to follow our operative procedures within the abdominal cavity.

ANTEOPERATIVE MANAGEMENT.—Aside from the general principles which govern the preparation of a patient for any major operation, certain special requirements are indicated which lessen the operative risk, and the tendency to postoperative complications in abdominal surgery.

Postoperative pneumonia, for instance, will occur less often if we make careful choice of the anesthetic for any given case, and if we make this period of anesthesia as short as possible, on account of the known tendency of some acute infections to shoot ahead when the patient is under the influence of ether or chloroform. Some operators will choose nitrous oxide and oxygen in cases in which this phenomenon is anticipated. In some feeble patients, or patients with complications of disease of vital organs, spinal anesthesia according to the Jonnesco method is desirable.

Preoperative intestinal asepsis can only be approximated, but for most practical purposes a good purgative given within twenty-four hours of operation will suffice. If the stomach itself is to be operated upon, further steps in the direction of asepsis are required, and we wash the stomach out very thoroughly with saturated boric acid solution just in advance of operation. This is done most comfortably, as a rule, after the patient is under the influence of the anesthetic, and by means of the common siphon tube. After the alimentary tract has been cleansed by purgatives, it is important to give only the simplest articles of food and drink in advance of the operation, but we must avoid having a patient abstain in such a way as to become unduly weakened. Patients who are accustomed to dieting may sometimes be placed on special diet to advantage for a few days in advance of operation, but the physical effect of placing a patient on diet for any length of time is apt to be such as to counteract any good effect.

Special stress has of late been laid on carbohydrate starvation as a cause of acidosis. It is important that an excess of ketone substances, acetone, diacetic, and oxybutyric acids (acetonemia, *q.v.*), sometimes with increased ammonia elimination, should be looked for by laboratory tests prior to operation.

> The expenditure of muscular energy before, during, and after operation entails a deficiency of glycogen which carbohydrate starvation only serves to aggravate, and which manifests itself by acidosis, with *dyspnea, tachycardia* and *acetone breath* as main phenomena. When acetone or di-

acetic acid is found in the urine in such cases, active treatment is indicated. Following Bainbridge's routine preoperative treatment the writer administers a **purgative** and for several days **milk sugar** and also **sodium bicarbonate** by **mouth** and **rectum,** to reduce the acidity of the urine to normal limits. In marked acidosis, large colonic irrigations of the same salt 6 to 10 quarts—liters—of a solution, 1 dram—4 Gm.—to the pint—500 c.c., are given daily, for the same purpose. Burnham (Amer. Med., Nov., 1916).

Inability to assimilate carbohydrates is best treated by supplying enough carbohydrate and by the neutralization of acid products with alkali. Surgeons must keep their eyes open to the dangers of acidosis. Prolonged starvation is especially harmful in children or those suffering from any form of exhaustion. W. A. Lincoln (Annals of Surg., lxv, 135, 1917).

It is far better to omit the cathartic or prepare the patient according to the following plan: Seventy-two hours before operation the bowels are cleared with **castor oil.** After the cathartic only liquids or food that will leave very little residue is permitted. In rectal operations, the evening before the operation the patient is given a high enema of **normal saline solution,** and 2 hours before operation a copious low enema of warm saturated **boric acid solution.** Fansler (Jour.-Lancet, Nov., 1920).

Preoperative Purgation.—This measure has recently been condemned by a number of prominent surgeons, who found its omission beneficial owing mainly to the fact that a purged bowel is often distended with gas and decidedly congested. Sajous has pointed out that purgatives sweep from the intestinal canal a product termed "secretion," by Starling, which not only serves to liberate and activate the pancreatic enzymes, but also to promote the production of bile and succus entericus. Normally, after about 24 hours this temporary deficiency adjusts itself; if, however, an operation is performed, this readjustment is retarded in proportion with the shock involved. Again, Sajous having shown that the intestinal enzymes are bactericidal and antitoxic, their elimination by purgatives tends to favor autointoxication and fermentation.

In general a short period of rest in bed before an operation is of advantage, but if this time extends beyond twenty-four hours, excepting for patients who are already in bed with some severe abdominal complication, the apprehension and introspection of the patient with a negative imagination in advance of operative procedures may be disastrous, and has even gone to the point of allowing the patient to develop suicidal impulse. For patients who are not already in bed from necessity, the author prefers to have as short a period of preparation as expediency would suggest, not more than twenty-four hours as a rule. There are many instances in which the patient needs special medical treatment in advance of operation, because of some defect of the heart, lungs, or kidneys, but under such circumstances with most patients it is best not to tell them of the date set for operation far in advance, up to which they are to be led.

The prognosis of preoperative shock is materially improved if **an hour or two is allowed for resuscitation prior** to operation, during which **saline solution** is given subcutaneously or by vein, **warmth** applied, an opiate injected, and **camphor in oil** given subcutaneously if a stimulant is required. Prior to operation it is well to give **omnopon** and **scopolamine.** The best anesthetic was found to be warm **ether** and **oxygen.** Lockwood, Kennedy, Macfie and Charles (Brit. Med. Jour., Mar. 10, 1917).

Anteoperative narcosis is undesirable for one chief reason shown by Cantacuzene in his experiments with animals subjected to the influence of opium after infection. This author

showed that narcotized animals rapidly succumbed at the time when another series subjected to the same infection, but not narcotized, were meeting the infection.

Arrangements should be made beforehand for maintaining the animal warmth of the patient with woolen garments or blankets, and it is best to have a good circulation of air in the operating room. In an overheated operating room with closed windows and doors the surgeon himself may be extremely uncomfortable, and feeling the need for oxygen, and we assume that the patient at the same time suffers the same depressing influence in addition to the shock of the operation. Experiments with animals have shown that the peritoneum is not injured by exposure to air currents and to low temperature as much as it is injured by contact with gauze, antiseptic solutions, or by rough handling. The author believes that the temperature and air circulation of the room most agreeable to the surgeon is at the same time most beneficial to the patient. Asepsis is to be begun where possible before the operation with a general bath, and particular attention given to the preparation of the umbilical region.

The skin in the field of operation may be well prepared in the common way by shaving, then scrubbing with green soap, which is washed off with a weak bichloride of mercury solution, and a pad of gauze wet with this solution is placed in contact with the wound for a few hours. A more recently used and very effective way of sterilizing the skin consists in simply painting it over with a 2 per cent. solution of iodine in benzin after shaving. The need of aseptic surroundings

relating to the preparation of the operating room need not be discussed in this article. Asepsis on the part of the operator is met by the wearing of a sterile gown and cap and a mouth guard of gauze, because with every breath, and particularly in the course of conversation during an operation, bacteria are projected from the mouth of the operator over the field of the wound.

The hands and forearms may be prepared simply by scrubbing with green soap, and then in a weak solution of bichloride of mercury. This destroys practically all of the bacteria which are likely to cause trouble. Latent colonies of bacteria which work out of the epithelium of the hands in the course of an operation are generally dormant colonies which are managed by the blood-serum or tissues of the patient safely. The use of rubber gloves in abdominal surgery is particularly undesirable; first, because they interfere with the nice sense of touch required for separating adhesions, or for doing rapid suturing. The operator wearing rubber gloves is apt to require longer incisions which allow him to work by sight, and this is not in harmony with the principles of the physiologic era in surgery.

The peritoneum protects itself so well if given fair opportunity that we do not need to apply the extreme degree of asepsis that would be needed in opening the knee-joint or the meninges of the brain, but it is well for assistants who are not engaged in separating adhesions, or in applying sutures, or in hunting for structures within the abdomen, to wear rubber gloves. One can do a much higher class of operative work

within the peritoneal cavity where nice sense of touch is not interfered with; and the greater length of time required in operating where rubber gloves are used and the longer incisions counterbalance the benefit of such asepsis as would be gained through the use of the gloves.

It has been shown experimentally with Petri plates in the operating room that large numbers of bacteria are constantly falling into every open wound, no matter what precautions have been observed in advance. These bacteria are for the most part disposed of in the patient's tissues and blood- and lymph-vessels; but the longer the incision and the greater the length of time during which any given wound remains open, the more bacteria fall into the wound from the air.

If one can work more quickly and through shorter incisions with bare hands, he naturally makes better asepsis of the wound, provided that his hands have been well prepared in advance.

Instruments may be sterilized by dry heat in the oven, by immersion in 95 per cent. carbolic acid, or in the more common way by boiling in water for fifteen minutes. In the latter case bicarbonate of soda in the proportion of a teaspoonful to a quart of water is added to prevent the rusting of instruments. The carbolic acid preparation is particularly suitable for small, sharp, delicate instruments, and does not interfere in any way with their edges. The carbolic acid which clings to them on removal is instantly neutralized by immersion in alcohol.

INSTRUMENTS AND APPARATUS.—Scissors.—There are very few intra-abdominal operations which cannot be performed from first to last with a pair of scissors and a couple of needles and no other instruments whatsoever. In adding other instruments which give special facility in certain operations it is well to remember this statement, and it will avoid the multiplicity of instruments which are frequently used to the patient's disadvantage or injury, as may be observed often enough. The form of scissors which the author prefers is the ordinary French locked type, five or six inches long, with one sharp point and one blunt point, and kept very sharp. The preference for scissors over scalpel is based upon the fact that small blood-vessels seem to ooze much less after division with the scissors than with the scalpel. This is possibly due to contraction stimulated by the character of the cut made by the scissors, but there is no interference with primary union of the tissues subsequently, according to observations extended over a series of years.

Needles of the Hagedorn type will suffice for practically all abdominal work, and needles threaded with catgut slipped under bleeding vessels readily take the place of the artery forceps without loss of time, with a rather greater degree of accuracy, and with less crushing of tissues. For intestinal or gastric suturing the author prefers a needle that is considerably larger than the one that is commonly used, for the reason that it carries a suture of greater diameter, and a suture of fairly large diameter does not cut out of the tissues so readily as an extremely fine suture when subjected to tension. The custom of using a very fine needle

and silk is based upon the idea of causing the least degree of operative damage and avoidance of leaking of contents of the hollow viscera, but it is not based upon our observations of the extent to which the mucous membrane will plug fairly large punctures, or our knowledge of the greater security of tissues sutured with a strand large enough to bind without cutting.

Retaining Apparatus.—The author is in favor of depending upon his fingers, and those of assistants, rather than upon clamps and other retaining apparatus in abdominal work; but this is because his methods were acquired while many of the proficient clamps which facilitate these procedures were in the course of development, and which gave mechanical advantages which seemed attractive, but which were sometimes observed to be injurious. Rubber-covered clamps of various forms, if carefully used, allow one to work speedily. One may not make such accurate adjustments or such regular insertion of sutures if he disposes of mechanical adjuncts, and yet in cases where he can work quite as quickly without them the balance of advantage is in favor of the gentler method. Temporary steadying sutures may sometimes be employed in addition to the fingers in order to maintain a viscus in a certain position while operation is being performed, and these are liable to do less harm than steel instruments in the peritoneal cavity. The author has employed most of the mechanical devices described for facilitating operative work upon the stomach and bowel, but has dropped most of them, excepting the Murphy button, in favor of simple methods of suturing, and the button is not used

nearly as often now as it was a few years ago.

Drainage tubes for the most part should be small, as otherwise they play the part of a foreign body in the abdominal cavity, and this is resented by the peritoneum. In 1895 the author described, in his book on the subject of appendicitis, a drainage wick which would take the place of drainage tubes in most places in the peritoneal cavity, and which would cause very little offense to the peritoneum. It consisted of gauze rolled loosely in a covering of gutta-percha or of rubber dam, very much as one rolls a cigarette, but leaving one end of gauze protruding. This soft, flexible drainage wick acts by capillarity, adapts itself to bends and angles, and suffices for most purposes of abdominal drainage, provided that one understands the principles of capillary drainage, and keeps a good mass of fresh gauze upon the abdominal wall in such a way as to maintain the capillary power of the wick.

Gauze drains not protected with an inoffensive covering are quickly filled with lymph-coagula poured out from the peritoneum in response to their irritating presence, and they become fastened to tissues in such a way that on removal they may draw loops of bowel into angulation. Where a very long drain is required, as from the cystic duct or from the bottom of the pelvis, the same principle may be applied by using an ordinary flexible-rubber drainage tube or catheter split throughout its entire length on one side, and the wick of absorbent gauze carried loosely through the lumen of the tube. It is very seldom at the present time that one will need to use any gauze packing in the peritoneum

cavity; but if such a calamity does arise, less harm is done if the gauze is covered with an apron of gutta-percha tissue or rubber dam to keep the bowel from becoming adherent, thus carrying out in a way the principle of the protected drainage wick. For patients with very heavy abdominal walls where pressure might nearly close the wick drain with its cover of rubber dam, or of rubber tubing, sheet lead is a useful part of our apparatus. Sheet lead can be cut with the scissors into strips of any desired width or length, and this strip doubled upon itself carries between the two arms a drain of absorbent gauze. The end of lead projecting upon the external abdominal wall can be bent over to avoid the danger of the drain slipping within. Lead seems to be quite as benign as rubber or gutta-percha tissue, and is accepted kindly by the tissues, excepting where it projects to some distance within the abdominal cavity, in which latter case it presents a more rigid and objectionable foreign body.

> Sheet rubber is superior to gauze sponges in abdominal operations. It eliminates the danger of leaving a sponge in the abdomen as well as the local acapnia due to contact of the moist sponge and the resulting shock, a condition demonstrated by Henderson. Rubber sponges also eliminate the tendency to form adhesions, so easily induced by the use of gauze. The wound itself heals more easily and the after symptoms of discomfort are markedly decreased. Sterilizing of the sheet by boiling is easy. J. W. Keefe (Jour. Amer. Med. Assoc., Aug. 19, 1916).

Suture Materials.—The choice of suture materials in abdominal surgery is extremely important.

For ordinary ligating of vessels,

and for suturing of the peritoneum where adhesions are to be avoided, very simply prepared catgut is preferable, and excepting for large vessels a catgut which would be absorbed in forty-eight hours possesses advantages, because any suture material for the peritoneum which remains for two or three days is prone to cause, by its irritating presence, a line of peritoneal lymph-exudate followed by annoying adhesions. This is in accordance with the well-known action of the peritoneum in walling in any object which is a source of irritation. While such adhesions may be absorbed later, and may not be in a position to cause much annoyance, nevertheless there are many thousands of patients today suffering to some degree from adhesions of the omentum or bowel to the anterior abdominal wall, in cases where this complication could have been entirely avoided by the use of very fine, quickly absorbed suture material, which would not have caused the pouring out of much lymph by the peritoneum. Peritoneal margins united with the finest of sutures become adherent so quickly that there is no real need for any suturing which will last for more than twenty-four hours in the parietal peritoneum of the abdominal wall, or in other places where strong permanent adhesions are not purposely induced.

For suturing the cut margins of bowel or stomach for the purpose of preventing hemorrhage, and of closing of tissues against infection, small chromic catgut in the place of simply prepared catgut is desirable, for it resists digestion when in contact with the secreting glands of these organs longer than simply pre-

pared catgut. Simply prepared catgut, when in the secreting glands of the stomach or bowel, may be liquefied in a very few hours, and chromic catgut in this position will do no harm, because it is at a point where adhesions are purposely secured.

Linen thread and silk are used in the positions where we wish snug apposition of tissues until firm adhesions have been formed, or cut structures of the stomach or bowel have united. For closing all parts of the abdominal wall we may dispose of any suture material, excepting the very fine, simply prepared catgut for the peritoneal layer and skin, and chromic catgut for the anterior and posterior sheaths of muscles; but, in place of chromic catgut where a lasting, yet absorbable material is desired, the author is very fond of kangaroo tendon. It is remarkably benign in the tissues, which receive it with such a degree of toleration that large strands are carried readily, and the kangaroo tendon lasts in the tissues for a longer time than chromic catgut, unless the latter is prepared in a way which makes it so hard as to be irritating.

LOCAL ANESTHESIA.—The dangers attending general and even spinal anesthesia in greatly weakened or moribund patients are being increasingly recognized, and corresponding attention is paid to **local anesthetic methods.** Lennander pointed out that, in general, anesthesia of the abdominal wall and parietal peritoneum is alone necessary to permit of intra-abdominal surgery, and upon this basis the indications of local anesthesia have been gradually extended in this field.

No operation under general anesthesia should be performed on an adult which can equally well be done under local anesthesia, in view of the greater safety of the local procedure.

The writer blocks off the line of incision by completely surrounding the area with a barrier of 0.5 per cent. **novocaine** (procaine) solution to which 3 to 5 drops of 1:1000 **adrenalin** solution per ounce have been added. The peritoneal cavity having been entered, the patient makes no complaint, unless tugging and pulling on the viscera are indulged in. Local anesthesia is particularly indicated in the presence of alcoholism, nephritis, myocarditis, and acute myocarditis, but is also well suited for such operations as suprapubic cystostomy, gastrostomy, enterostomy, cholecystostomy in debilitated patients with gall-bladder empyema or severe obstructive jaundice, appendectomy in tuberculous patients, all hernia operations, and operations for typhoid perforation. Vomiting seldom follows such anesthesia, and food can be taken shortly after the operation. J. H. Jacobson (Jour. Mich. State Med. Soc., xv, 57, 1916).

The toxicity of **novocaine** is dependent upon the strength of solution rather than upon the total amount used and its comparative safety makes possible the use of the drug in large quantities. Perfect anesthesia results in negative intra-abdominal pressure, producing postmortemlike repose which permits visual examination which is, of course, preferable to digital. The contraindications to local anesthesia are largely limited to: (1) psychic incompatibility; (2) pathology adherent to the posterior parietal peritoneum; (3) adherent malignant disease; and (4) very high-lying gall-bladders. Abdominal packs are not needed except to prevent soiling, orientation being obtained by the negative intra-abdominal pressure, vertical retraction, etc. There is a very marked decrease in such postoperative discomforts as gas, nausea, and vomiting with the resultant wound strain. Children of all ages lend themselves well to the method. The time required is greatly reduced by use of the pneumatic injector, 2 to

5 minutes being all that is necessary with proper technique, after which the operation may be begun at once. If the anesthesia becomes inadequate, general anesthesia may be resorted to at any time. R. E. Farr (Journal-Lancet, xxxvii, 353, 1917).

Exceptions to the rule that parietal anesthesia is alone necessary for abdominal operations are the lesser omentum, the cystic and common bile-ducts, the portal vessels, the renal capsules, and the ureters, all of which are sensitive (also the pelvic and diaphragmatic peritoneal surfaces).

Preliminary injections of **morphine and scopolamine** are very useful, and often practically indispensable in extensive operations under local anesthesia.

Our associate editor, W. Wayne Babcock, recommends a 1 per cent. **novocaine** solution for the skin incision and a 0.25 per cent. solution for the deeper tissues.

In the splanchnic analgesia a wheal is raised 7 cm. from the midline at the lower border of the twelfth rib. A needle 12 cm. in length is passed through along the horizontal plane of the body, and introduced obliquely forward so that it makes an angle of about 45° with the median plane. When it strikes the vertebra, about 9 cm. from the point of entrance, it is drawn back and then reintroduced at a smaller angle. As soon as the point is felt gliding along the surface of the vertebra it is pushed in 1 cm. further. At this point 25 to 35 c.c. of 1 per cent. **novocaine-adrenalin solution** are injected after it has been ascertained that no blood comes out of the needle. This procedure is then repeated on the other side. G. L. Labat (Brit. Jour. Surg., viii, 278, **1921).**

POSTOPERATIVE TREAT-MENT.—The patient on being returned to bed should have wool next the skin and hot bottles at the extremities, even though not much shock be present, for shock is present to some degree after almost any abdominal operation, due to stimulation of the afferent nerves of the

brain and cord centers, with more or less lack of vasomotor power. There is apt to be more or less perspiration from leaking sweat-glands when the patient is placed in bed, and any undue exposure at this time may lead to a chilling which would be inducive to postoperative pneumonia. For the first twenty-four hours approximately the disturbance of the intimate ganglia of the bowel will usually result in derangement of function of the bowel so that any food material is apt to undergo fermentation instead of digestion, and the toxemia from such fermentation may be very injurious, and might give rise to serious complications.

Thirst is inseparable from the postoperative period, and **hot water** given in teaspoonful doses frequently will partially allay the thirst, and supply all the real needs of the stomach for some hours after the operation. Patients are very urgent at times in their demands for cold water or ice after an operation, but cold water has a distinct tendency to increase vomiting, and ice in the mouth produces the same reaction that cold does upon the skin, as one observes after making snowballs: the hands become red and irritated, and in the same way the mucous membrane of the mouth and pharynx becomes irritated, if the patient is allowed ice or ice-water, excepting in the most minute quantities.

The **injection of** a quart of **normal saline solution into** the **lower bowel** immediately at the close of the operation and while the patient is still under the influence of the anesthetic, has also been recommended for the relief of thirst. The patient is elevated to the moderately high Trendelenburg posture, a stiff rectal tube inserted well up into the sigmoid flexure, and the

fluid slowly poured into a glass funnel, held 3 or 4 feet above the level of the buttocks. John G. Clarke found that this procedure also reduced to a minimum the vesical irritability, so common in operative cases. EDITORS.

Diet.—The first food to be borne after the hot-water period is passed is liquid diet and predigested milk, or fermented milk of several kinds, and broths are usually well borne. In two or three days, if the temperature and other vital signs are fairly normal, a more liberal diet will allow the patient to regain strength more rapidly. Meteorism, which is usually present to some extent, with or without colic, because of the disturbance of the sympathetic ganglia of the abdomen, may be relieved ordinarily if stimulating enemata are given; but for the most part it is well to leave the patients pretty much alone, without attempting to do too much for them during the first twenty-four hours after an abdominal operation. Many times the author has asked patients what they most desired during the first day after an abdominal operation, and the common answer has been that their greatest desire was to be left alone.

Opiates.—There is a general tendency to give opium in some form after abdominal operations, if the patient is in pain, but we must remember the specific action of opium in lessening the resistance to the spread of infection immediately after an operation, and not apply mistaken efforts at kindness in wishing to quiet the patient's pain. There are some patients of nervous temperament who suffer so much and who are so restless that they tire themselves out with fretting, if we do not give opium in some form.

Consequently the resource is one that we may be obliged to use, but it should not be used excepting with full knowledge of its danger. It is the author's habit to tell patients in advance of operation that they are going to suffer a great deal afterward from colic, nausea and pain, but that they will arrive at a comfortable stage soon afterward. The effect of this statement to the patient has never, so far as the author knows, deterred anyone from having an operation done, as there is the natural feeling of pride in being able to meet such conditions, and the patient, expecting a good deal of trouble immediately after operation, and prepared for it, is frequently enough surprised to find it so much less in degree than had been anticipated.

Where the patient recovers quickly from the anesthetic and vomits or becomes restless, ⅙ grain (0.01 Gm.) of **morphine sulphate** may be given hypodermically. If he sleeps out of the ether, it is not necessary until later. **Rectal saline,** 1 pint (500 c.c.) should be administered slowly before the patient recovers from the anesthetic, or immediately after. **Water,** either hot or cold as best tolerated, is given as soon as the patient asks for it. H. W. Jones (N. Y. State Jour. of Med., xvii, 458, 1917).

Insomnia is so dependent on stomach and bowel disturbances that the two belong closely in association. Insomnia which is dependent upon the disturbance following an operation is not so distressing if the patient has a good nurse who suggests quiet in all of her movements, and who does not allow avoidable disturbances to keep the patient awake. Sleep will be established frequently in a natural way by the third night. Part of this insomnia at night is due to the fact

that patients doze off at various times during the day, and really get during the twenty-four hours about all of the sleep that is necessary. A number of ordinary hypnotics, avoiding the opium preparations, will give some relief, and this is a matter which must be left to the judgment in individual cases rather than stated in the way of a general rule.

POSTOPERATIVE COMPLICA-TIONS.—Shock when severe in degree requires special treatment in addition to the customary methods for retaining the body heat and keeping hot bottles at the extremities. Elevation of the foot of the bed temporarily allows the heart to work with less effort, but we have to be guarded about suddenly lowering the foot of the bed at any time while the patient is still in a condition of shock. The patient at this time may be suffering from one of two kinds of anemia: anemia due to lack of vasomotor power and perhaps also anemia due to direct loss of blood. For the anemia due to loss of vasomotor power secondary to derangement of function caused by disturbance of the sympathetic ganglia of the abdomen strychnine is indicated, and should be given hypodermically in doses of from a thirtieth to a twentieth at intervals of about four hours.

For the anemia due to actual loss of blood the indications are for supplying the loss of blood temporarily, and this is done either by direct transfusion of blood or more commonly by intravenous infusion of normal saline solution. In cases in which we have both kinds of anemia present at the same time the use of the strychnine may be quickly transitory and injurious, unless we have first by transfu-

sion or infusion given the heart and blood circulatory system the mechanical advantage of possessing a full complement of fluid.

The use of saline solution by rectum is protested against by the writer, who found a transient albuminuria to result from this procedure in a large series of cases. Plain water should be given by rectum instead. Comparative tests showed that one-third more fluid is thus absorbed, and that less water is required by the mouth. Trout (Surg., Gynec. and Obstet., May, 1913).

Basing their conclusions on 356 operated abdominal penetrating wounds, the writers consider camphor in oil the best cardiac stimulant; pituitrin intramuscularly in half-ampoule doses aids peristalsis and eserine is also often of value for this purpose. Two hundred Gms. (6⅔ ounces) of saline solution, with or without 30 Gms (1 ounce) of brandy, should be given by rectum every 3 hours as a routine in all cases and continued for 2 to 3 days. Small sips of brandy or champagne, or ½ Gm. (8 minims) of tincture of iodine in 4 Gms. (1 fluidram) of water usually controls hiccoughs. Lockwood, Kennedy, Macfie and Charles (Brit. Med. Jour., Mar. 10, 1917).

Adrenalin or digitalis are powerful stimulants, but they stimulate the heart out of proportion, and are very transitory in effect, and unless given with great caution may lead to overstimulation, especially if given in conjunction with strychnine. Overstimulation will be followed by secondary shock coming on a few hours after apparent recuperation from the first evidences of shock. Bandaging the legs firmly in order to drive out the blood in part and give the heart less work is, like elevation of the foot of the bed, a resource of temporary value, but we need to be guarded about removing the bandages before

recuperation from the condition of shock is well established.

The best method of administering the suprarenal principle, according to A. J. Walton, is by continuous rectal injection in **saline solution,** 1 dram of **adrenalin** solution to a pint of saline, *i.e.,* 1 in 160,-000; the temperature of the liquid should be between 108° and 112° F., and it should not flow in faster than 1 pint an hour. Crile found that by giving **adrenalin** continuously, the circulation of a decapitated animal could be maintained ten and a half hours.

Hypodermic injections are absorbed very slowly during severe shock, but intravenous injections of **adrenalin** or of **pituitary extract** raise the blood-pressure more than in the normal state. A single injection of an extract of the posterior lobe of the pituitary was found by Mummery and Symes to influence arterial tone for upward of an hour.

> Six cases of gall-bladder and appendix disease which, from 36 hours to 2 weeks after operation, though apparently convalescing nicely, developed symptoms of acute myocarditis with dilatation of the heart. This is believed due to secondary infection, operation exciting streptococci in the gall-bladder, they having a selective affinity for the heart muscle. A stock vaccine or antitoxin might be developed from the gall-bladder or other organ involved and used in each case. E. A. Vander Veer (Trans. Amer. Surg. Assoc., June, 1917).

Meteorism of extreme degree also appears to depend upon two chief factors: partial paralysis of the muscularis of the alimentary tube due to disturbance of the sympathetic centers, and to fermentation of contents of the alimentary tract caused by saprophytes, which gain ascendancy when the normal control occurring in the course of undisturbed digestion is taken away. The meteorism secondary to mechanical obstruction or of

spreading peritonitis includes these same prime factors, but the different forms of this condition require treatment based upon causation in the individual case. The meteorism which is due to simple shock calls for mechanical treatment chiefly, although the fermentation of intestinal contents is relieved to some extent by the use of **subgallate of bismuth** as an intestinal antiseptic, and by the use of the **lactic acid ferment,** consisting of prepared cultures of the *Bacillus Bulgaricus,* which now may be obtained in tablet form, or which may be used indirectly in milk prepared by the action of this bacillus.

Mechanical resources consist, in ordinary cases, of introducing a **rectal tube** to allow the early escape of gas, and by **abdominal massage** applied gently but persistently, beginning at the right side over the cecum and carrying the massage along the entire course of the colon. This order of massage movements seems to relieve distention of the small bowel quite as well as the colon, probably because of the natural tendency toward emptying of the small bowel into the colon. In the presence of severe colic in meteorism, massage would seem to be contraindicated, but it is not, because colic is due to a spasm of the muscularis of the bowel in its effort to contract to the normal caliber, and massage movements seem to give to the bowel the same sense of security that is obtained by a splint in cases of fractures attended with muscular spasm of the extremities.

The author is impressed by the fact that treatment of meteorism of the bowel in this way by massage and by the rectal tube is not commonly appreciated as it should be, and he has very

many times afforded decided and lasting relief by these resources.

A hypodermic injection of $\frac{1}{50}$ grain (0.0013 Gm.) of **eserine salicylate** gives excellent results, according to F. E. Taylor, in tympanites after colotomy. Within fifteen minutes the patient begins to pass flatus. An enema of **sulphate of magnesium** should then be administered. If necessary, the injection may be repeated in six hours.

Acute dilatation of the stomach belongs to the same category, is probably dependent upon the same causes as meteorism of the bowel, and has practically the same order of complications. In many cases there seems to be selective impression made upon the innervation of the stomach by shock, perhaps because of its proximity to the solar plexus, and dilatation of the stomach occurs out of proportion to dilatation of the bowel. When we recognize acute dilatation of the stomach by the persistent vomiting, distress, and visible distention of the upper left quadrant of the abdomen in excess of distention of other parts of the abdomen, we have the characteristic features of this form of meteorism. In this condition the mechanical features of treatment are all important, and are obtained by placing the patient **prone** upon the abdomen, with the result of causing constant compression of the distended stomach. With the patient in this position, the stomach tube introduced at frequent intervals, **washing of the stomach with warm saline solution** results in causing the escape of very large quantities of gas. Patients suffering from this condition are not so sensitive to the introduction of the stomach tube as many others, and the immediate relief which is given temporarily often makes them eager

for the next introduction of the tube. The important matter is to apply the stomach tube often enough, and this is a point commonly neglected. We must keep the stomach empty of gas and fermenting contents.

In cases in which the patient happens to rebel against introduction of the stomach tube because of highly sensitive fauces we may spray the fauces in advance with cocaine solution, and, if the tube is lubricated with a nice quality of sweet oil to which is added a few drops of wintergreen, the patient, relishing this, will chew the tube for a few moments, and then begin swallowing it. Further advance of the tube is made by the surgeon.

Meteorism due to mechanical obstruction of the bowel is also met with. At the present time we see very much less of dynamic and adynamic ileus than we did some years ago, when it was common practice to use gauze packing in abdominal surgery. This gauze packing lowered the patient's general resistance, as a foreign body in the peritoneal cavity. It caused excessive exudation of plastic lymph from peritoneal surfaces, and adhesion angulation was a frequent feature in consequence, or if not angulation, the arrest of peristalsis from the involvement of the long segments of the bowel among adhesions.

That form of ileus in which peristalsis progresses violently up to the point of arrest with a rapid production of grave symptoms can oftentimes be relieved by **posture.** If the patient's hips and legs are elevated upon the back of a chair which has been placed upside down in bed, and gentle massage applied, gravitation will sometimes stop the angulation or

kinking of bowel in a few minutes, and it is gratifying to see the whole picture of a desperate case change so rapidly as it sometimes will when this posture resource is being applied, together with gentle massage. Reopening of the abdomen and a search for the point of mechanical obstruction are such very fatal procedures that they must not be employed with much hope of obtaining relief, but some authors hope, which the author does not share freely, to secure an occasional good result by opening the distended bowel by incising it after reopening the abdominal cavity to allow the escape of gas, or by injecting sulphate of magnesia solution through trocar punctures in the bowel. Clinically I think that we may usually observe that when the bowel is opened at any point for the escape of gas it allows the escape of gas only in the immediate vicinity, the paralysis of the bowel preventing the contraction necessary for emptying the lumen at more distant points. Rapid opening of the distended bowel at a point above the obstruction, insertion of a drain to carry off the poisonous contents, and subsequent operation for the relief of the obstruction, after the patient has made some gain, is occasionally successful.

Our resources must be applied promptly in cases of ileus with meteorism, because toxins generated in any part of the bowel which is not emptying itself rapidly lead to a dangerous toxemia, and the colon bacillus particularly increasing in virulent culture in an obstructed or paralyzed part of the bowel may not only cause general toxemia, but may be carried to the kidneys and liver, and there give origin to a train of

serious complications discussed under the next heading.

> Thirteen cases of acute gastric dilatation during operation. All but 1 were relieved by prompt passage of the **stomach tube.** All postoperative cases with more than the usual emesis should receive gastric lavage. When dilatation has developed, repeated gastric lavage must be carried out. In extreme cases the patient should be placed in the knee-chest position to facilitate complete evacuation. E. Novak (Jour. Amer. Med. Assoc., lxxvii, 81, 1921).

Colon Bacillus Nephritis.—If this continues after relief from the ileus has been obtained, it will require special treatment internally. Five grains of **benzoate of soda** combined with five grains of **hexamethylenamine** administered at rather frequent intervals, according to the judgment of the physician, will exert a specific influence upon the complication of colon bacillus nephritis which so commonly follows conditions that entail loss of control over this bacterium. When the benzoate of soda and hexamethylenamin internally do not control colon bacillus nephritis in a satisfactory way, the pelvis of the kidneys may be flushed through a ureteral catheter.

In many cases one may state incidentally that colon bacillus nephritis is often enough present in advance of operation in many abdominal conditions, passing for ordinary nephritis, unless one devises means for determining if the colon bacillus is present, and the author has known of instances in which excellent consultants wished to postpone operation because of the presence of albuminuria, when, as a matter of fact, this albuminuria was due to the presence of the colon bacillus, and to be cured only after removal of the focus of

original infection by the abdominal operation. The colon bacillus nephritis which occurs with appendicitis may often clear up rapidly after the operation without any special treatment directed to the nephritis, and the same result may be anticipated in a certain proportion of the cases of colon bacillus nephritis occurring with ileus.

Meteorism due to extension of peritonitis after operation is sometimes treated by the old Clark opium method, which consists in placing the patient profoundly under the influence of **morphine.** It acts by limiting the spread of peritonitis due to peristaltic movements of the bowel, and the loss of resistance on the part of the patient from the shock which goes with peritoneal pain. On the other hand, we have the objection that bacteria increase more rapidly in a patient under the influence of opium. In addition to the beneficial influence of opium in selected cases, the **ice-coil** placed on the abdomen has the tendency to lessen the spread of peritonitis besides limiting the pain.

The author has preferred the principle of turning the blood-current toward emunctories of the bowel, and securing elimination of toxins along with a free watery discharge from the mucosa of the bowel. This is accomplished fairly well by the high rectal injection of an ounce of **alum** in a quart of water. The alum in the bowel produces the same effect that it does in the mouth, causes rapid watery secretion from neighboring glands, and incidentally stimulates contraction of the paralyzed bowel, with emptying of its contents. We might anticipate that alum would have in the bowel an astringent effect, with

the tendency to cause constipation, but it has precisely the reverse action, and the great amount of watery exudate which is drawn out in the presence of alum seems to overcome any irritating effect which it might have.

Sulphate of magnesia by high injection has an effect like alum, of causing watery evacuation which presumably carries off toxins, and the influence of sulphate of magnesia is probably due to its hygroscopic nature, drawing fluids from the peritoneal cavity toward the bowel lumen by osmosis. The sulphate of magnesia injection, either alone or combined with **glycerin,** which is also hygroscopic, is perhaps the favored method of obtaining movement when there is any degree of paralysis of the bowel, but the alum injection is much more effective, and will act in cases where paralysis is established to such a degree that sulphate of magnesia would exert no apparent influence. In addition to these rectal injections, a very gentle **massage** is effective in some cases in overcoming the paralysis of the bowel, although it seemingly would be contraindicated. In cases where septic peritonitis is present at the time of operation, and there is danger of such peritonitis remaining as a postoperative complication, the Murphy **proctoclysis** is invaluable. This consists of the very slow instillation of warm saline solution into the rectum continuously for a long period of time, and many forms of special apparatus for the purpose have been devised. The apparatus of Dr. Robert C. Kemp maintains an even temperature of the saline solution by the use of the vacuum principle in the container of the fluid, similar to that

obtained by the thermos bottle. The methods here described for treating cases with spreading peritonitis assume that we have made provision for sufficient drainage and have applied other resources in an operative way.

> As **laxative enemas to be used,** when necessary, after abdominal operations, the author mentions the following: (1) **Magnesium sulphate,** 2 ounces (60 Gm.), in water at 102° F. (38.3° C.), 1 pint (500 c.c.). (2) **Glycerin,** 2 ounces, in water at 102° F., 1 pint. (3) **Castor oil,** 2 ounces, in acacia emulsion (½ ounce—15 Gm. —of acacia to the pint of water). (4) **Oxgall,** 20 grains (1.3 Gm.), and glycerin, 1 ounce (30 c.c.), in starch-water, 1 pint (500 c.c.). Winslow Anderson (Pac. Med. Jour. Sept., 1916).

> In postoperative ileus and intestinal paresis, the writer uses an enema of 1 dram (4 c.c.) of stronger **ammonia-water** in 1 pint of water, the effect of which is greatly enhanced by a hypodermic injection of **pituitrin,** 16 minims (1 c.c.), half an hour previously. T. A. Black (Med. Rec., Apr. 1, 1916).

Poisoning by bichloride of mercury and by iodoform have in the past been common postoperative complications, although at the present time they do not occur so frequently, but still require attention. Poisoning by bichloride of mercury through absorption from large wound surfaces gives rise to the characteristic irritation of the mucosa of the alimentary tract, but seldom appears in abdominal work, because there is almost no situation in which an expert operator would think of using bichloride of mercury. Iodoform, however, is very frequently used in abdominal surgery, but chiefly with iodoform gauze, and this gives rise to iodoform poison-

ing so frequently that the author on one occasion, when being asked to look for it in a hospital ward, found several cases unsuspected in one ward. Iodoform is taken up very rapidly by the peritoneum, and its symptoms are commonly mistaken for the symptoms of septicemia, with rapid pulse, wet skin, and peculiar mental wandering.

Where we have occasion to suspect that iodoform poisoning is a postoperative complication in abdominal work, we may determine the point by adding a pinch of calomel to some of the patient's urine in a saucer, and stirring with a wooden spatula. If free iodine is present in the urine it makes the customary reaction to iodide of mercury, distinguished at once by the cloud of color. Removal of iodoform gauze from the wound in such a case, and taking up iodoform which is adherent to the tissues by pouring **sterilized oil** into the cavity from which the gauze was removed, and leaving the oil there for some minutes before abstracting it with absorbent apparatus, will commonly allow the patient to recover from a severe case of iodoform poisoning.

Patients vary greatly in their susceptibility to iodoform, and the author observed one death from iodoform poisoning with characteristic signs in a young girl, sixteen years of age, in a case in which he arrived too late in consultation. And the young girl had been poisoned by a roll of iodoform gauze, not much larger than two fingers in size, after an appendix operation. The surgeon in charge had been absolutely at a loss to account for the symptoms. While there are positions in which iodoform

gauze is of considerable value in small quantities in abdominal work, we must always bear in mind the danger of the postoperative complication of iodoform poisoning.

Skin eruptions seen frequently after abdominal operations, were found by F. J. Shepherd to occur most often in patients receiving an enema of soapsuds made from common yellow soap. When Castile soap was substituted no eruption followed. Cheap, yellow soap contains a considerable quantity of resin, and to this he ascribes many of the rashes seen after abdominal section.

Uncontrollable vomiting immediately following operation is probably due to excessive stimulation of the nerves of the stomach through shock, or from the irritation of ether which is being excreted by the glands of the stomach, and it seems to be due also at times to reversed peristalsis of the upper part of the bowel, throwing contents of the duodenum into the stomach, with continuance of the wave of reversed peristalsis to the point of including the entire stomach. This complication sometimes becomes so dangerous that we must stop it by the chief means at our control, giving the patient the harmful **morphine.**

If vomiting persists after 12 hours, the author gives 1 dram (4 Gm.) of **sodium bicarbonate** in 6 ounces (180 c.c.) of lukewarm water. This washes out the stomach and usually results in cessation of vomiting. Rarely does it become necessary to resort to the stomach tube. In any case, sodium bicarbonate in doses of 20 grains (1.3 Gm.) every 3 hours is helpful for the first 2 or 3 days. It not only overcomes the acidosis, but appears to have a favorable influence on gas pain. H. W. Jones (N. Y. State Jour. of Med., xvii, 458, 1917).

Properitoneal hernia is sometimes the cause for ileus with its vomiting and other train of symptoms, but it is not likely to occur in cases in which the operator is aware of the danger of this complication, and has guarded against it. Properitoneal hernia occurs in cases in which there has been defective suturing of the peritoneal layer of the abdominal wall after operation, and a small knuckle of bowel is forced by vomiting or cough into the space between the peritoneum and the muscular layer of the abdominal wall.

Hernia into a rent in the omentum may occur as a postoperative complication, and, if, in the course of separating adhesions, the operator has left any small openings in the omentum, these should be extended clear to the margin of the omentum, or closed by suture. In any event, possibility of hernia complication should be foreseen in all work which deals with the omentum, if rents are left unclosed.

Perforation of the bowel sometimes occurs as a postoperative complication at the site where a rigid drainage tube or bulky drainage apparatus has caused an undue amount of pressure, and perforative ulcer may occur a few days after the operation at the site of a gastroenterostomy, if the bowel has been fastened so far away from the pylorus that acid contents of the stomach escape directly into the bowel at the point of juncture.

Postoperative phlebitis occurs often enough to require attention. It may appear two weeks after an aseptic operation, and its origin is not well understood. As a postoperative complication in appendicitis, it sometimes

appears as an inflammation of the left iliac vein or left saphenous vein, and occurs in fact at a distance quite as often as at the site of operation. While causing a high degree of discomfort and prolonging the period of illness, it is not often an absolutely dangerous complication. If abscesses are formed, they are apt to remain localized rather than to give rise to septic embolism.

Pylephlebitis does not often occur as a postoperative complication, excepting in cases in which we have evidences of its presence in advance of operation, but abscess of the liver may appear so late after an abdominal operation that the relationship between the primary focus of infection in the peritonal cavity and the liver abscess may be lost sight of. A patient may even leave the hospital, and his home, and travel to a distance for recuperation, with beginning abscess of the liver, the treatment for which will receive consideration under the heading of that subject.

Secondary abscess may appear at the site of an infection which has been cared for at the time of operation, but such secondary abscess is prone to liquefy newly coagulated lymph toward the external abdominal incision, and to follow this line of least resistance, rather than to extend in other directions.

Mesenteric thrombosis not markedly present at the time of an operation may increase to become a postoperative menace, due probably to injury of the veins in the course of an operation, but the complication is rare.

Bladder complications do not call for special consideration in this article. The bladder sometimes refuses to contract in a normal way after various abdominal operations. This is sometimes due to nothing more serious than the unaccustomed recumbent position of the patient, or to psychic influence, although shock sometimes leads to disturbance of the innervation of the bladder, and at the same time we are apt to have hyposecretion of urine due to a similar influence upon the kidneys. It is best to avoid using a catheter if possible for emptying the bladder, and it is seldom necessary, excepting when we have direct evidence of an overfull bladder. Otherwise it is best to resort to such resources as massage of the bladder above the pubes, and the sound of trickling water upon a warm bedpan placed beneath the patient. If we begin too early to use the catheter, there is a tendency for the bladder to depend upon that resource for some days, and sometimes for as long as the patient remains in bed, if we begin with the mistaken idea that prompt use of the catheter will simplify matters.

Postoperative psychoses occasionally occur after abdominal operations, and the operation is commonly held by relatives of the patient to be the primary cause. Such disturbances usually mean the precipitation of impending psychoses which were developing in advance of the operation, but kept in check by the will of the patient until the shock and surroundings of the operation relaxed that control. Such psychoses may be due to central causes, but are also sometimes toxic in origin, as the abdominal surgeon sees them, and such psychoses precipitated by operation may be really on the road to elimination, due to removal of the origin of the toxic impression.

Peritoneal adhesions causing trouble subsequent to operation receive consideration along with that general subject elsewhere in the article.

Postoperative pneumonia occurs, according to various authors who have tabulated many thousands of cases, in from 2 to 5 per cent. of all abdominal operations, although in practice one may have series of one or two hundred operations without a single case of pneumonia, and it is very much less frequent today as the result of our refinement in technique than it was ten years ago. True croupous or lobar pneumonia, lobular pneumonia and hypostatic pneumonia may all stand in direct relationship to causes which are more or less under control by the surgeon. The development of true lobar pneumonia, developing immediately after an operation, seems to the author to be more than a coincidence. The disturbance incident to any abdominal operation may lower the vitality of the patient in such a way that the omnipresent pneumococcus may suddenly spring into activity, particularly if ether has been the anesthetic. We have recent knowledge that infections of various sorts may begin quickly in animals under the influence of that anesthetic. The shorter the period of anesthesia, and of operative procedure which lessens general resistance, the less we shall probably have of true lobar pneumonia, which has generally been held to be merely coincidental.

Hypostatic pneumonia after abdominal operations may appear for the same reasons that it appears elsewhere, but neither hypostatic nor true lobar pneumonia are so distinctly traced as postoperative complications

as is lobular pneumonia, and this lobular pneumonia is the particular one with which we usually have to deal. According to statistics, lobular pneumonia occurs more often after abdominal operations on the aged, and more often in men than in women, but the latter feature of the statistics does not have special reference to abdominal operations. While general anesthetics are all more or less irritating to the bronchial mucosa, and postoperative vomiting is a factor allowing aspiration of mucus or substances from the stomach, there are other features leading to a special preponderance of lobular pneumonia after laparotomy. The pain following abdominal operations interferes with full range of the muscles of respiration and favors pulmonary stasis, but direct infection of the lungs by bacteria may occur in three ways: by way of the mucous membrane, the blood- and lymph-vessels. After abdominal operations, with a tendency to pulmonary stasis because of limited respiration on account of abdominal pain, and retention of matters which would be expectorated if coughing were not so painful, bacteria arriving at the lungs from the abdominal region by way of the blood- and lymph- vessels meet with resistance which is less than normal. The author believes that long exposure of the peritoneum in the course of an ordinary operation may lead to the carrying of large numbers of air bacteria indirectly to the lungs without complete destruction *en route* by phagocytes, and it is his impression that these cases are not infrequent. Embolic pneumonia and its common sequence of lung abscess by infection through the

blood-stream no doubt occurs from the handling of thrombosed vessels, and, while we recognize certain cases of pneumonia directly due to the presence of the larger emboli, it is probable that we have many other cases in which minute emboli give rise to complications which appear a few days after operation.

Pleurisy frequently follows operations upon the liver and gall-bladder, if these operations are for cases with infection. Here it is probable that infection is transmitted by way of the lymphatics through the diaphragm to the pleura, and the neighboring lung becomes next infected, giving us sometimes the dangerous pleural pneumonia. The postoperative complication of pleurisy or of pleural pneumonia cannot well be guarded against, but we may anticipate the danger of postoperative lobular pneumonia, and lessen this complication very distinctly in several ways: by avoiding as far as possible unnecessarily prolonged operations with the accompanying long period of anesthesia; by maintaining the body warmth of the patient, and by allowing the patient postures which favor expectoration. It is probable that the Fowler position after operation, while not particularly favoring expectoration, may lessen the danger from embolic pneumonia to some extent.

Fistulæ from the alimentary tract and bile-tract are sometimes annoying as postoperative complications, but when not formed purposely for useful purposes they have a remarkable tendency to close spontaneously if left alone. Very much harm is done almost as a matter of routine at the present moment by surgeons, house staff assistants and nurses in their efforts at keeping such fistulæ carefully cleansed. Antiseptics introduced into such fistulæ cause disturbance of the delicate new cells which are being thrown out for purposes of repair, and even so harmless a solution as saline solution is commonly injurious in fistulæ. Employment of hydrogen dioxide, which cleanses fistulæ in a most attractive way, is one of the most injurious of resources, because it destroys new cells quite as readily as it destroys pus. In cases in which we have reason to suspect that a fistula is kept open by something at the bottom of the fistula, as a knot of unabsorbed ligature, a concretion, a bit of fecal matter, or other foreign body, we shall usually need to operate, for efforts at closing such fistulæ are usually very futile until the foreign body is out.

Excepting in cases in which we believe that a foreign body lies at the bottom of the fistula, our treatment had best be a treatment of neglect, doing nothing whatsoever in the way of cleansing the fistula, and simply using an external dressing for the purpose of cleanliness. Under this treatment new repair cells quickly form connective tissue, and such connective tissue, according to its well-known habit, contracts regularly and closes fistulæ. There are a few cases in which epithelium will move downward from the skin and upward from the bowel, forming an epithelial covering for the walls of a short fistula, and when such short fistulæ are seen to have an epithelial lining this may be destroyed by leaving 95 per cent. carbolic acid along the line of the fistula for half a minute, and then neutralizing it with alcohol. After

the destruction of epithelium in this way by carbolic acid, new cells are formed, but we must be sure that epithelial cells do not again cover the surface, and to guard against this the highly astringent subsulphate of iron is effective as an astringent which will not allow new epithelial cells to grow, but which does not prevent the development of connective-tissue cells, although connective tissue formation in such cases is tedious.

One of the most persistent fistulæ in the author's practice followed an operation for perforating ulcer of the duodenum, in a patient whose large size and desperate condition did not allow detailed work at the ulcer site at the time of operation. This fistula discharged pancreatic secretion, bile and chyme for some months, but finally closed spontaneously. As a rule, it is best to allow the patient with a postoperative fistula to get out of bed as soon as the wound is secured in the ordinary way, and the patient then goes about his ordinary occupation and engages in all sorts of activities, with no attention to the fistula beyond the wearing of a small external pad of gauze for the purpose of neatness.

Objects left behind after abdominal operations have led to complications in imposing array among statistics, and the gauze pad has been the chief offender.

The foreign body may cause, according to Schachner, an acute or a low and protracted form of sepsis; be encapsulated and retained for months or years; be extruded through the wound, or into the hollow viscera; or, more rarely, through the cicatrix.

Proper organization of the operating room prevents mishaps. Absolute quiet is essential, with well trained assistants each assigned to a particular task. Each instrument and piece of gauze should be accounted for. Some surgeons are apt to plead extenuating circumstances, but this occurrence occasions great suffering and a probable lawsuit. Nature tends to protect itself from the foreign body, and it may pass off through the rectum, but often a secondary operation is necessary. J. B. Deaver (Trans. Amer. Med. Assoc.; Med. Rec., Aug. 10, 1918).

When one or more objects have been left behind in the peritoneal cavity the patient may go on to recovery, but usually there is a persistent nausea and a higher degree of local tenderness and discomfort than we can usually account for, and the persistence of such condition of nausea and distress at the site of an operation may lead one to feel that it is best to reopen the abdominal cavity and search for a foreign body which has been left behind. This postoperative complication is not so easily guarded against as one might imagine; but gauze for intra-abdominal work, to which tapes have been attached, in the form of a long roll, one end of which is always left outside of the abdomen to guard against accident, should be employed.

The danger of leaving sponges is eliminated by the author by **dispensing with sponges** and using a single band of **sheet rubber** 8 inches wide and 18 feet long. J. W. Keefe (Med. Rec., July 8, 1916).

Secondary hemorrhage as a postoperative complication occurs more often in abdominal surgery than elsewhere, because of violent vomiting, which dislodges sutures and ligatures. This must always be borne in mind, and we avoid the accident by introducing as few mass ligatures as

possible, and ligating vessels separately. Very many cases of secondary hemorrhage have occurred after ligation of the broad mesentery of the appendix, or of a broad ligament, because contraction of the psoas and iliac muscles, in addition to the other muscular contractions in vomiting, has a tendency to broaden out the peritoneal base and force off such ligatures, unless they have been tied with caution. Secondary hemorrhage occurs also when violent vomiting has caused fine sutures of silk or thread to cut out under tension, and for this reason the author favors sutures of larger caliber than are commonly employed. Where large vessels have been opened, and secondary hemorrhage occurs marked by the ordinary signs of increasing thirst, restlessness, pallor, pain and rapid pulse, we must reopen the abdominal cavity for securing bleeding points and removing blood, and this is usually a very dangerous procedure because of the condition of the patient, requiring preparation for direct infusion of blood or introduction of intravenous saline solution at the moment the abdomen is reopened. Another form of secondary hemorrhage occurring after operation is common when the force of the arterial pulse is sufficient to give *vis a tergo* to blood in veins torn in separating adhesions, and which are not bleeding much at the time when the operation is completed.

After any aseptic abdominal operation considerable blood may escape into the peritoneal cavity without causing a great degree of disturbance beyond the increase in local pain, which is the characteristic sign of such hemorrhage. Aseptic blood in the peritoneal cavity is still in the circulation in a way, because the peritoneal cavity is a lymph-chamber, and the serous remains of the blood which escape in the course of coagulation are taken up into the blood circulation again. **Morphine** lessens the hemorrhage and strychnine increases it. Bearing these facts in mind, we may sometimes give the dangerous morphine to advantage, or withhold the strychnine unless it is greatly required.

There are 3 chief explanations for failure of relief of symptoms after operation:

1. The cause of the original symptoms was extra-abdominal and operative treatment was a therapeutic mistake. In this group frequent causes of error are pneumonia on the right side associated with pleurisy which, because of referred pain in the abdomen, is diagnosed as appendicitis, and pulmonary tuberculosis with gastric symptoms simulating gastric ulcer.

2. An intra-abdominal lesion giving symptoms was present, but was not recognized by the operator and the wrong operation was done. In this group careful exploration of the abdomen may show that gastric symptoms were due to an encapsulated pelvic abscess or an old ectopic pregnancy, that ureteral colic was the cause of appendiceal symptoms, or that a case thought to be a fibroid uterus was not helped by removal of fibroids because the real trouble was a carcinoma of the splenic flexure.

3. The operation was a technical failure because it either failed to do what was intended, added new pathological conditions which caused a continuation of the old symptoms, or created new symptoms. In this group are mentioned removal of epiploic appendices for the vermiform appendix, partial removal of the appendix leaving an infected stump, gall-bladder surgery in which a stone low in the common duct is overlooked, operations for visceroptosis failing to give the desired result. W. Wayne Babcock (Med. Rec. c, 319, 1921).

**TOILET OF THE PERITO-
NEUM.**—The peritoneum protects
itself so well, if given opportunity,
that we need pay very little atten-
tion to securing asepsis of any part
of the abdominal cavity while we
are at work. If pus escapes upon
normal peritoneum when abscesses
are opened, it commonly causes no
harm, even though it be left upon the
peritoneum when we are through
with the operation. There are two
reasons for this. Bacteria are chiefly
at work in the tissues rather than in
the pus proper, and the latter is often
practically sterile, even in the presence
of advancing infection. By pus I do
not mean intraperitoneal fluids teem-
ing with bacteria, but these are for
the most part not walled in like pus.
The principle, however, of treatment
is practically the same; for where
such fluids occur any special effort at
securing asepsis would be futile,
and, more than that, likely to be
harmful.

We may quickly arrange drainage
for such septic fluids, but efforts at
wiping or washing them out are apt
to lead to injury of the endothelial
covering of the peritoneum, and to
defeat the object of our good inten-
tions.

When fluids carrying bacteria or
sterile pus in quantity should be re-
moved, it is best to do it very gently
by quick absorption into masses of
absorbent gauze, rather than by
sponging or flushing, and we take
good care at the same time to avoid
the wiping which injures endothe-
lium. Where stomach or bowel con-
tents are likely to escape in the
course of an operation, it is well to
protect the field with absorbent
gauze, but such gauze adheres quickly

and firmly to normal peritoneum, with
injury to its endothelium. Where we
can apply the resource of placing a
layer of rubber dam between perito-
neum and gauze while we are at work,
we guard the peritoneum in the best
way. The peritoneum, while pro-
tecting itself remarkably against in-
fective material, is disabled by the
washing and wiping commonly em-
ployed, and particularly by the appli-
cation of germicides, almost any one
of which in the peritoneal cavity is
productive of damage.

A peritoneum which would be per-
fectly safe, even though considerable
septic fluid were left upon it, may
when disabled start out on a career
of infection which would have been
avoided if we had not tried in a crude
way to make the peritoneum ideally
clean. In the vicinity of the focus of
infection within the peritoneal cavity
a local hyperleucocytosis becomes
established with extreme rapidity,
and this does away with the necessity
for much of the work in toilet of the
peritoneum described by authors in
general.

There are occasions in which it is
desirable to evacuate very large
quantities of pus or septic fluids
quickly, and for this purpose **hydro-
gen dioxide** may be used, provided
that all exits are kept free, and that
the only peritoneum with which it
comes in contact is peritoneum al-
ready damaged. Hydrogen dioxide
damages normal peritoneum instan-
taneously, and is to be used only
where the peritoneum has already suf-
fered great damage, but in such situa-
tions it throws out pus and septic fluids
in a great foaming mass, and, this
mass removed, **saline solution** may
follow, leaving the cavity very clean.

While **hydrogen dioxide** is germicidal, its value rests in its mechanical effect in throwing out albuminous fluids and débris rapidly, rather than in securing asepsis where it is not needed, and when efforts to secure it through the use of germicides are damaging. For most cleansing purposes in the peritoneal cavity **physiologic salt solution** is the best, although even that is to be used with caution. If it is not employed with too much force or removed too vigorously it has a field of value. The solution of nine-tenths of 1 per cent., isotonic for human blood-serum, is more benign than the commonly employed six-tenths of 1 per cent. which is isotonic for frogs' blood, and which had its origin in the laboratories. The saline solution should be sterilized by boiling.

Sterile water, even though boiled, should never be used within the peritoneal cavity unless it contains salt. The reason why water without salt should not be used is because it is corrosive. Its corrosive nature may be noted at once by dropping it in the eye, which leads to immediate smarting and burning of the conjunctiva. Water without salt is so destructive to delicate tissues in laboratory work, and the fact is so well known, that it is a strange omission on the part of many authors to neglect to state the dangerous character of water without salt.

The reason why even sterile pure water is corrosive is because an osmosis of salts from the body cells immediately occurs in the presence of water not containing those salts in the proportion in which they are found in the body cells. Chloride of sodium, however, being the chief salt involved, is the only one which we need to add to the water for practical purposes in routine work.

Dawbarn poured milk representing septic fluid into the peritoneal cavity of a cadaver, and then set to work to find the best way to get all of the milk out again, and after a very great deal of flushing and sponging found that some milk still remained.

This showed how impossible it is to remove the septic fluid by any mechanical toilet of the peritoneum, and demonstrates the degree of damage to peritoneum which will occur incidentally through our efforts. Consequently the toilet of the peritoneum is best left in part to the peritoneum itself, aided by such resources as we have learned do not cause damage. As the result of experimentation some authors have closed the peritoneal cavity completely without drainage in cases in which it was known that some septic areas remained behind, depending upon the peritoneum to dispose of any sepsis after the chief focus of infection had been removed. While primary union often occurs in such cases, the author believes that at the present time it is best to use small capillary drainage apparatus for removing culture fluids from the septic site.

DRAINAGE OF THE PERITONEAL CAVITY.—Because of atmospheric pressure upon the abdominal contents, any free fluid within the peritoneal cavity has a tendency to follow the line of least resistance to the surface, and if this fluid is given direction by way of small capillary drains we fulfill the general indications in drainage, but posture of the patient is an aid under some cir-

cumstances; and the Fowler position, in which the upper part of the body is raised in bed to an angle which will allow fluids to gravitate to the drain in the lower part of the abdomen, is at times very useful. The only objection to the Fowler position is the call for rather more work on the part of the heart in a very weak patient.

In the upper part of the abdomen we have a natural mechanical situation, aiding drainage from the bile-tract region, in what is known as Morison's pouch, the space between the liver, above, and the stomach and colon, below. Blood, bile or septic fluids escaping into this pouch have a tendency to make their way directly to the surface at this point, instead of spreading into the general peritoneal cavity below, and this tendency is so marked that a very little capillary drainage carried to the bile-tract region suffices to clear the area of culture media. It even allows us to do away with suturing the common bile-duct in many cases in which this has been opened for removing a calculus.

Abdominal drainage is well conducted by any of the means described under the head of drainage apparatus, and the author feels that it is always best to employ capillary drainage, rather than drainage through tubes which carry no gauze wick. When a tube without gauze wick is filled with fluid, the column of fluid in the tube exerts hydrostatic pressure of considerable degree, which is met by the atmospheric pressure of the viscera, to be sure, but drainage through a simple tube cannot be so free as when fluids are guided through the tube by absorbent gauze with its high degree of capillary power. Drainage apparatus should be carried as little as possible among intestinal loops, because such drainage apparently acts as a foreign body, and the peritoneum rapidly throwing out lymph because of the offense seals in such drainage apparatus and deprives it quickly of its usefulness.

If the abdominal work carries us to the pelvis, there is sometimes an inclination for the surgeon to add vaginal drainage, because the Douglas pouch represents the lowest part of the abdominal cavity, and one would naturally feel that fluids would all gravitate to this lowest point. This is not quite true, however, in practice, as atmospheric pressure has a tendency to force even pelvic fluids to the midline incision in the abdomen, with or without encouragement from capillary drains, and the advantage of depending upon drainage through an abdominal incision rather than through a vaginal incision depends upon the comparative ease with which the area of the abdominal incision is kept aseptic. Drainage in the vaginal region is in an area much more difficult of maintaining in a degree of relative asepsis.

The author formerly felt that it was an advantage to insert drainage apparatus at more than one point in the abdominal wall at points that seemed natural places for collection of peritoneal fluid, but of late years, in a series of many hundreds of abdominal operations sufficient to demonstrate the real requirements, he has found that one point for drainage in the lower abdomen will suffice, and the only additional point used for drainage for many years has been in reference to Morison's pouch, which

amounts practically to a separate cavity more distinct than the cavity of the pelvis so far as the question of the necessity for drainage devices is concerned. We need to give aid to a single incision drainage at times by the addition of posture.

In order to carry out the principles of capillary drainage it is essential for one to be familiar with the mechanical principles involved, and to make frequent change of the external mass of gauze to keep the capillary drain at work within the abdomen. In cases in which fluids drained from the peritoneal cavity are irritating to the skin, the skin may be dried temporarily, and then covered in the vicinity with a thin layer of collodion or of vaselin. In addition to the drain for the peritoneal cavity, it is important, on closing the abdominal incision, to leave a tiny wick drain for twenty-four hours, extending between the muscle layer and the skin. This can rest between the sutures in such a way as to interfere not at all with final primary union. At the end of twenty-four hours, or at the time of the first dressing, it may be pulled out, and will be found to have drained out as a rule quite a little serum or free fat, or both, which would have been a menace as a culture medium. Excepting in patients with a very thin adipose layer, it is well to make it a rule to introduce this tiny drain at any convenient point between the sutures, and to remove it on the following day.

Drainage is indicated, in general, (1) where there is infection which in the absence of drainage would persist or extend; (2) where it is necessary to wall off by adhesions a portion of peritoneum; here the irritation results in adhesions and the formation of a pocket unconnected with the general peritoneal cavity. A commonly used drain consists of a rubber tube surrounded by gauze and this, in turn, by rubber protective. Wick may be passed into the inner tube and later removed, or the tube may be emptied at short intervals by the insertion of a smaller tube and aspiration with a syringe. In situations where a soft drain would be compressed to the point of obliteration or be soon disarranged, a glass drainage tube may be employed, e.g., in the pelvis or some deep focus to be drained through a mass of intestinal coils. Mikulicz's gauze envelop drain consists of a square of gauze pushed down into the wound, and into which gauze strip is packed. It is especially useful where, besides drainage, pressure packing for hemorrhage is also necessary. The inner packing may be replaced at intervals.

Removal of drainage should not be undertaken while infection is still present at the bottom of the cavity being drained. On the other hand, it must not be postponed to a point where the discharge drained is solely that resulting from the irritation by the drainage device. Usually adhesions are sufficiently firm for the removal of the drain after two days. Sometimes it can be removed in twenty-four hours. EDITORS.

Drainage should be removed early in all patients who are slow to react from an abdominal operation. In no case should gauze be allowed to remain in contact with the alimentary tract longer than twenty-four hours. Swope (Amer. Jour. of Obstet., Nov., 1915).

In applying the Ochsner treatment in septic abdominal states, the writer favors the Fowler position only in pelvic abscesses and in general peritonitis. A drain to the most dependent part of the abscess, in conjunction with turning the patient on his face and elevating the foot of the bed for ten-minute periods twice daily, aids in clearing the pelvis. In abscesses not in the pelvis, the Fowler position should not be used, but the patient turned toward the affected side, and once or twice a day turned over on the face to throw the pus

against the line of incision. A. M. Willis (N. Y. Med. Jour., May 29, 1915).

Drainage with the patient in the prone position tried out very successfully. The patient is placed on the abdomen usually for 24 to 48 hours, with the head of the bed elevated about 10 to 12 inches. One pillow is placed under the lower part of the chest and one under the head. There are no spaces in the front of the abdomen to favor the formation of pockets, as there are in the pelvis and alongside the spine, and the pus is brought against a part of the abdomen where blood-vessels and lymphatics are not nearly as numerous. Placing the patient on the right side was found very efficient. A pillow is placed under the region of the liver and the patient is turned far enough over so that pus will drain from in front of the left kidney. Among 15 cases of appendicitis treated in the lateral position there was no mortality. Among 42 cases treated in the abdominal position there were but 2 deaths. Among 47 cases treated in the Fowler position there were 5 deaths. Hill (Annals of Surg., lxvi, 414, 1917).

War surgery has taught what should be the 2 main principles of civil surgery: 1. Early and complete operation. 2. That secondary or mixed infection is worse than primary infection. While the tissues of the body can, if given a fair chance, deal with one infection only, if that infection becomes a mixed one by entrance of organisms from outside, then the last state is worse than the first. If surgeons will take their courage in both hands, and will not be frightened by a little infection, leaving it to be dealt with by the natural resistance of the tissues to infection, and will give up the use of drainage tubes, they will not only find their results much better, but also their outlook on surgery totally changed. All that is necessary is to put something into the tissues which will keep a "passage" open but which

does not leave an open "drain." The writer puts in a piece of soft folded rubber—for instance, in an appendix abscess. This allows pus to come away, but will not leave an open "drain" by which secondary infection of staphylococci, from the skin, or other organisms can gain entrance. Hathaway (Brit. Med. Jour., June 29, 1918).

HEMOSTASIS.—A few technical points belong to hemostasis in abdominal surgery. Where it is possible to use torsion instead of ligatures—and this covers very much of the field— we can avoid ligatures, the presence of which causes the peritoneum to throw out plastic lymph in the vicinity for its protection, very much as the mollusk throws a layer of nacre over a grain of sand in the shell. Where it is necessary to use ligatures we avoid including much mass in the ligature, because, the larger the mass, the greater the tendency for the peritoneum to throw out reparative lymph which will lead to adhesion formation subsequently. We have also to remember that the efforts of vomiting after an abdominal operation have a tendency to pull off certain ligatures, and consequently we must leave a considerable mass of tissue outside of the knot. Such mass of tissue is not likely to slough, as some operators fear, because it is kept alive by lymph circulation in the vicinity, and has a tendency to gradually become absorbed in a very benign way, because of the fact that it is tissue belonging to the individual. Hemostasis of the cut margins of the alimentary tract cannot readily be obtained by ligating, and consequently we employ the suture here instead, for the most part, and snugly drawn running sutures suffice for the purpose.

Gauze moistened with saline solution is to be preferred for sponging during the operation. Larger, flat gauze sponges, previously warmed, are employed to cover and hold aside intestinal coils. Rubber tissue may with advantage be placed between the gauze and peritoneum to minimize irritation of the latter and subsequent adhesions. Pressure with gauze is effectual in arresting capillary oozing.

Permanent arrest of bleeding by the temporary pressure of a hemostat and clot formation cannot be relied on, as the clot may later be forced out when the blood-pressure rises to normal. Aside from ligature, the cautery is, in rare instances, required. In the case of deep vessels that cannot be ligated, but are caught with clamps, the latter may be left in place, surrounded by gauze and rubber tissue for two days, then cautiously removed. Gauze packing may likewise be left *in situ* for a time. EDITORS.

EXTERNAL INCISIONS.—The ultimate success of an abdominal operation often depends largely upon the choice of the external incision, and we have two especial points to bear in mind: consideration of the best route for getting to any objective point within the abdominal cavity, and at the same time the best way for avoiding imperfect repair of the abdominal wall and unsightly scars.

This includes a consideration of avoiding nerves which supply muscles, because a temporary or permanent paralysis of certain abdominal muscles was a very annoying post-operative complication before surgeons began to give attention to this matter. To reach an objective point in the peritoneal cavity, and at the same time avoid the complication due to muscles cut transversely, we may practically cover the ground by stating that it is well to plan to make separate division of each layer—skin, adipose tissue, fascia, muscle and parietal peritoneum—and, further, to make blunt dissection as far as possible of each muscle, even though this sometimes leads to openings crossing each other at somewhat different angles. Stretching of the muscle wound with the fingers, however, does away with most of the awkwardness of a situation where split muscles, after blunt dissection, as it is called, lie at different angles.

When, for any reason, it becomes necessary to cut transversely across a muscle we must mark well the point at which such transverse incision was made for the purpose of making accurate repair subsequently, otherwise the muscles acting in their lines of traction during the course of the operation will smooth out angles more by transverse incisions, and it is difficult to restore these angles again. On general principles our incisions are to be made directly over the objective point, but because of the ease with which an incision is made into the abdominal cavity in the median line, and the ease with which such an incision is repaired, the midline incision should be used for perhaps the larger part of our abdominal work.

The size of incisions will depend largely upon the operator. One must make as large an incision as he needs for working freely and safely, but, if experience allows an operator to make his incisions shorter and shorter safely in any particular field of abdominal work, the patient will have the advantage of less danger from subsequent hernia, less shock, and less noticeable scars. Small incisions are dangerous for the beginner, and plenty of room is desirable on his account, but he may adopt the middle

ground of beginning with a comparatively small incision, and then enlarging it as occasion requires.

If the abdomen requires opening in two different localities at the same sitting, there is frequently an advantage in making two or more small separate openings, rather than extending a large one to reach distant points, such as often occurs in cases of intestinal obstruction, where one is not sure of the point of the obstruction. If through the first incision, in a case of obstruction, one does not readily reach the point at which the constriction occurs, he is likely to add much more to the serious condition of the patient if he makes a large incision and pulls the bowel out from that than he is if he makes more than one incision small, and then passes the bowel between his fingers at that point without drawing it out upon the abdominal wall. Special incisions will be noted in connection with certain operations, the above covering only a general principle.

When we have occasion to open the abdomen at the site of a former operation, it is well to carry the incision through normal skin on either side of the scar line for two reasons: because of the advantage of removing the scar tissue in some cases, and because in opening at the site of an old scar one may run across adhesions of abdominal viscera of which he was not aware, and they may be injured. The safe way for entering along the site of an old scar, and for leaving the viscera in good condition for repair subsequently, is to go down through normal tissue on either side of the scar until muscle sheath is definitely reached, and then snipping muscle sheath until the muscle beneath is seen.

The sheath can then be opened freely on either side of the scar without danger. If there is any question about adhesions being present at just this point of dangerous character, we extend the incision through the sheath of muscle to some point above or below the scar, where we may enter the peritoneal cavity at a point free from adhesions, being extended at a free point large enough to admit the finger. The finger is then carried back along the peritoneal side of the scar line, and adhesions if present are separated. This having been done, the posterior sheath of the muscle and transversalis fascia and peritoneum are safely cut along the entire line of the scar, and the parts left in excellent position for correct apposition subsequently.

In the typical vertical incision, or median postmuscular incision, no motor nerves or muscles are divided. Firm muscular protection is assured by making the openings in the deep fascia to one side of the median line and retracting the rectus muscle outward. Laterally, the best incisions are of the muscle-splitting type, the fibers of each muscle encountered being separated longitudinally and the nerves identified and protected. Transverse incisions are usually such only through the skin and superficial fascia, though Willy Meyer has recommended, for free access to the stomach, a transverse incision in which one or both recti are cut across and later reunited. EDITORS.

The Perthes rectangular flap method is favored for many operations in the upper abdomen by the writer. An incision is made in or near the median line, beginning close to the xiphoid and running straight down nearly to the level of the umbilicus: here a turn is made and the incision carried horizontally to the anterior axillary line. In the vertical part all tissues are divided down to the posterior sheath of the rectus. At the lower end, the second and third fingers of the left hand are passed

beneath the rectus until the outer edge of its sheath is felt. Then 2 parallel rows of horizontal sutures are passed through the rectus and overlying fascia and tied. Between them the muscle is cut and the horizontal incision completed, the corner of the flap being next raised with a sharp retractor while the operator separates the skin and muscle flap from the underlying aponeurotic layer in the direction of the costal arch. This is done with a gauze pad. When the two intercostal nerves with their associated vessels appear this part of the dissection is completed and the abdomen is opened by an incision through the aponeurosis and peritoneum parallel to the costal arch and close to it. The incision gives free access to the upper abdomen, preserves innervation of all the tissues, has the skin and peritoneal incisions at different points, and permits extension in either direction. Willy Meyer (Jour. Amer. Med. Assoc., Nov. 17, 1917).

For operating on the rectum and on the pelvic ureter, the author advises a skin incision beginning at the symphysis pubis, running in the midline upward for about 2 inches, then diagonally upward and outward toward the anterior superior spine. The fascial incision repeats the direction of the skin incision. The rectus muscle, thus exposed, is freed and divided between clamps. Care is taken to push back the epigastric vessels from the posterior surface of the muscle, and to clamp, divide and ligate them separately. The fascia of the transversalis and obliquus internus and the peritoneum are then divided by an incision which repeats the direction of the skin incision. In closing, the peritoneum, with the transversalis and internal oblique fascia, is sutured by a running stitch. The divided rectus may be approximated by mattress sutures. The anterior sheath of the rectus and fascia of the obliquus externus muscle are closed by overlapping. J. W. Churchman (Annals of Surg., Feb., 1918).

One must always be on guard against small hernial protrusions into scar sites, and a small knuckle of bowel may be adherent in such protrusions without having led to symptoms sufficient for one to suspect its presence. Ordinarily, on reaching the peritoneum or subperitoneal fat, it is not necessary to pick it up and divide between forceps, if one has reason to believe that no adhesions occur at that point. Under ordinary circumstances, the various layers of the abdominal wall having been opened down to the peritoneum, or peritoneal or subperitoneal fat, these structures may be made tense between two fingers of one hand, the two points of scissors then introduced into this tense area nearly parallel with the plane of the abdominal wall, and an entrance into the peritoneal cavity made with celerity. This opening can then be enlarged to any desired extent with the scissors, or in many cases by stretching.

Closure of the abdominal incision may also be described in a general way to cover most of the principles involved. The first suture of the peritoneal incision should consist of the finest catgut, because, the smaller the strand of catgut, the less peritoneal irritation from the suture, and consequently less tendency to adhesions of the omentum which reaches out to wall-in points of irritation within its range. A fine strand of catgut is also a distinct advantage along the line that would be touched by the liver, which slides along the abdominal wall with each respiratory movement.

Placing a small, flat pad underneath the wound is helpful in holding down the intestines while the peritoneum is being

sutured; the pad is withdrawn when the peritoneal suturing is nearly finished. A continuous suture, with the needle inserted about ¼ inch from the margins, the serous surfaces of which should be held in apposition by stretching between hemostats, is used for the peritoneum.

Murphy proved that suturing an abdominal incision in layers gives a more satisfactory and stronger looking wound histologically than the *en masse* suture. Wounds sutured in layers were the stronger after two weeks, when the strength of the scar was tested by actual pull. The time necessary for repair is, moreover, decreased. Violent manipulations of the edges of an abdominal incision must be carefully avoided. Editors.

In experimental work with animals in the course of which the author closed peritoneal incisions with rather large strands of catgut or silk for the purpose of saving time, he observed that adhesions of intraperitoneal structures of some sort along the suture line are practically universal. He observed that the smaller the strand of catgut, the less postoperative adhesions occurred, and although such adhesions commonly become absorbed they remain just often enough in practical surgery to make it a very general point to avoid them as much as we can. Very little strength indeed is required for approximating peritoneal margins, and a suture which would be absorbed in forty-eight hours is all that is required, and a very small strand at that.

It is the sheaths of the muscles upon which we depend for strength when closing an abdominal incision. Suturing of the sheaths of the muscles is carried out neatly by using a continuous suture of chromic gut along the posterior sheath first, and then returning along the anterior sheath without introducing sutures into the muscle itself at all when the incision is made in the median line of the abdomen, and the same principle can be used in several parts of the abdominal wall. Muscle belly does not hold sutures so well as muscle sheaths, and there are few situations where it is necessary to introduce sutures into the muscle belly. By bringing the posterior and anterior sheaths of muscles into their respective normal positions, atmospheric pressure carries the bellies together much more evenly than we could do it with sutures.

Several fanciful methods for suturing the various structures of the abdominal wall have been described, but it is not necessary to do anything more than to leave structures as we found them as nearly as possible. Where one can catch the transversalis fascia along with the posterior sheath of a muscle in a suture, it is well to do so.

In cases in which there may be need for reopening the abdomen subsequently, interrupted sutures of the muscle sheath for a part or all of the way are of advantage, because then we reopen only to the extent necessary. Where a drain has been left in an incision, the suture running up to the drain may be followed by a provisional interrupted suture, if it is desired to close the incision completely when the drain is removed, but this is seldom necessary, for proper suturing up to the small drains which are now in vogue will allow of the walls falling together naturally enough when the drain is removed.

One disadvantage of carrying the sutures through muscle tissue is the danger of the sutures cutting through

such tissue when the patient vomits. This space then fills with blood which must be replaced by new tissue cells, and it usually is so replaced if the blood, as a culture medium, does not become exposed to infection from the suture, or some other source. For the muscle-fascia suture, chromic catgut or kangaroo tendon is desirable, because they last so much longer than simply prepared catgut, but not so long as to constitute a source of irritation, as a rule. Kangaroo tendon seems to be much more benign than chromic catgut, and it lasts rather longer in the tissues, unless the catgut has been chromicized in a way which makes it too hard.

In large wounds, figure-of-eight sutures of silkworm gut are also sometimes used, catching all layers superficial to the peritoneum. A few days later, when the danger of vomiting or other unusual strain has passed, and the fasciæ united, they may be taken out again. The deeper loop of the figure-of-eight embraces the deep fascia and the superficial loop all the remaining tissues over it. If used as permanent rather than tension sutures, these sutures should be inserted about ⅜ inch apart. EDITORS.

Where one needs to introduce interrupted tension sutures, there is nothing better than kangaroo tendon passed through muscle sheath, carefully avoiding the fat, into which no tension suture should ever be introduced. When closing the adipose layer of the abdominal wall, it is extremely important to avoid allowing any sort of suture to enter any fatty structure. The reason for this is because the entrance of any suture, or even the needle carrying the suture, into the adipose layer allows free oil to escape and to follow the course of the needle or suture, and such free oil, according to the principle of

hydrostatics, will begin to travel, opening up lines for infection in many cases.

Where a very small amount of oil is set free along suture lines it is no doubt absorbed in many cases, but nevertheless always introduces a danger which is unnecessary, because we can apply a principle in mechanics commonly overlooked which allows us to do away with any suturing through any adipose layer of the abdominal wall. This principle is the one which is employed by the boy who lifts stones after pressing down upon them a disk of wet leather to which a string is attached in the middle. It is the principle of making use of atmospheric pressure. When the suturing of muscle sheath has been completed, if the adipose layers of the abdominal wall are then pressed together with the hands, they adhere firmly under atmospheric pressure the moment that the skin is sutured. It is somewhat difficult at the end of forty-eight hours to separate fatty tissues along the original line, if one has occasion for any reason to re-enter the abdominal cavity. The question of suturing the adipose layer then may be disposed of by saying simply, *Do not suture adipose tissue at all.*

To overcome in most instances the difficulties of intra-abdominal operation in stout patients, the writer resorts to a large excision of skin and fat from the overweighted abdominal wall, removing a skin section either in the transverse or in a vertical direction corresponding to or at right angles with the incision, about 8 or 10 inches in length by 3 or 4 inches in width. This does away with the thickness of the wall down to the fascia, while from the fascia inward the difference between different ab-

domens is not great. If the patient is excessively fat, one will then naturally do a regular lipectomy operation. Kelly (Annals of Surg., March, 1911).

In suturing the skin the use of the subcuticular suture avoids scarring with a needle, and it also avoids the danger of making stab cultures of the *Staphylococcus albus*, which is found regularly as an inhabitant of the hairfollicles of the skin. Where very heavy abdominal walls are to be supported, we may fortify the skin sutures by placing squares of zinc oxide plaster at a short distance from the line of incision on either side of the incision, and then lacing these squares together through eyelet holes placed in the margins.

To avoid infecting the wound with the lacing, a thin layer of dressing is first placed next the wound, and then the squares of adhesive plaster laced together over this. We thus avoid altogether the necessity for introduction of deep through-and-through sutures, which in the past have been commonly used for supporting overheavy abdominal walls.

> Deep catgut sutures of the abdominal wall sometimes become absorbed before there is perfect union. To overcome this, the writer uses a silkworm gut slip-knot or running knot method. A Reverdin needle is passed through the edges of the two recti muscles; the middle of a strand of silkworm gut is pressed into the eye and the needle drawn back toward the operator. The two ends of the gut are then passed through the loop to form a slip-noose. Before tightening this a piece of silk thread is passed through the loop and its ends knotted together. This serves later to withdraw the loop. The noose is then pulled tight. The two ends of silkworm gut are now

passed through the skin margin nearest the operator through two needle holes made in a line parallel to the incision but about 2 to 3 cm. from its edge. The ends are then knotted. The skin margins not being brought closely together by the ends of the slip-noose, in the case of subcutaneous suppuration they can be separated without disturbing the deep sutures. When all the deep sutures are completed the cutaneous sutures are placed. About the tenth or eleventh day the slip-noose can be removed. This is done by cutting the two ends of the deep sutures immediately under the knot. Traction is then made on the silk thread and the loop easily withdrawn. H. Chaput (Presse méd., July 19, 1917).

To avoid unsightly scars of the skin due to stretching out and widening of the scar line after union is complete, we put a single layer of gauze or chenille over the line of incision, and then pour on collodion. This collodion-gauze dressing may remain in place for two or three weeks if one wishes, and it constitutes a very neat resource for avoiding scarring of the abdominal wall for people who have a perfectly legitimate vanity in the matter.

> Above the navel the transverse incision offers the most adequate exposure of the various pathologic conditions. The gall-bladder, stomach, and even the appendix, if not adherent in the pelvis, can readily be dealt with. In most instances retraction of the abdominal wall, both upward and downward, is possible so that good exposure is usually obtained. By supplementing this incision with the near midline vertical incision when necessary, one is afforded the most ideal exposure it is possible to obtain. R. E. Farr (Trans. Minn. State Med. Assoc.; Jour. Amer. Med. Assoc., Sept. 21, 1918).
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> The transverse incision used over 8 or 10 years by the writer, is par-

ticularly advantageous in some cases of gall-bladder trouble or diseases of the ducts; also in diseases of the stomach and pylorus, when one is not sure of the diagnosis. It gives splendid access to the organs in the upper abdomen. W. H. Magie (Trans. Minn. State Med. Assoc.; Jour. Amer. Med. Assoc., Sept. 21, 1918).

EXPLORATORY OPERATIONS.—
Very few exploratory operations should be done in abdominal surgery. The method no doubt makes diagnosis easier for the surgeon, but a more difficult matter for the patient, and it is highly important to make use of all available diagnostic resources before taking active steps in an operative way. Where an exploratory operation really needs to be done, however, it is best to make as small an incision as will suffice for the purpose. There are cases, for instance, in which we need to know if adhesions in the bile-tract region are complicating a loose kidney, or an appendix operation; and an exploratory operation, if small, for the purpose of determining that point is frequently in order. Then again, after traumatisms and perforations, the peritoneal cavity can contain blood, chyme, fecal matter or gas, which might be overlooked if one were too conservative about making exploratory incisions. In the presence of traumatic shock, ordinary diagnostic resources may fail us, and lead us to employ what older surgeons are apt to consider the resource of the tyro, namely, the exploratory incision.

To dress the wound a rectangular pad consisting of ten layers of gauze, fixed with straps of adhesive, and covered by an abdominal binder, constitutes a suffi-

cient dressing after short abdominal operations, though some operators use silver foil, collodion, an antiseptic powder such as aristol, or a wet dressing as an immediate covering for the incision. Where drainage has been instituted or infection is apprehended, some absorbent material may be also applied. On the seventh to the tenth day non-absorbable sutures may be taken out, but adhesive-plaster should again be firmly applied. Indeed, the adhesive and binder should be continued, as a rule, for four weeks after the operation, though healing is sufficiently secure for the patient to rise from bed in two weeks. EDITORS.

PERITONEAL ADHESIONS.—
Perhaps the most potent single factor in surgery of the abdomen relates to peritoneal adhesions. They lead to a large part of the constipation from which the public is suffering; to an extremely important part of the obscure dyspepsias; to various local areas of pain and tenderness, and frequently enough to acute disasters. The surgery of peritoneal adhesions belongs to the surgery of the future for the reason that such adhesions are commonly overlooked by diagnosticians at the present time, and only a trifling percentage of cases of gastric and bowel disturbances are placed where they belong in cause and effect relationship to adhesions. The new work of filling the stomach with bismuth solution and then making fluoroscopic examination to determine points of interference with gastric motility is now allowing us to make the diagnosis of gastric adhesions freely.

In post-mortem work we find peritoneal adhesions at some point in pretty much every abdominal cavity, in adults at least, and the argument that these have not caused trouble during the patient's lifetime includes

the idea that the patient is to have made the diagnosis himself, and to have informed his physician in the ordinary course of narration of his troubles. In this article the subject of peritoneal adhesions can receive nothing more than brief treatment, but it may be disposed of in a general way which includes most of the principles.

The surgeon has to consider the matter of separating peritoneal adhesions when they are found to give trouble, and to prevent their recurrence. He has to take steps in his operative work which will guard against the formation of adhesions resulting from his work. On the other hand, he has to resort to the use of peritoneal adhesions established for his own purposes in many parts of abdominal work. In cases in which we wish to make use of peritoneal adhesions it is important to scarify the peritoneum in the vicinity with the point of a needle in order to make sure of the free exudation of lymph together with destruction of part of the endothelial layer. The desirability of this scarification is experienced in laboratory work where one is working with animals, and it leads to the feeling that sometimes we do not obtain adhesions enough for safety in some kinds of bowel work, unless scarification has insured their production.

When we wish to prevent the re-formation of adhesions which had formed in advance of operation, many resources are of more or less value, but the author has chiefly depended upon two. These consist in the use of the aristol film, and the Cargile membrane made of the sterilized peritoneum of the ox. Aristol film is obtained by sprinkling aristol freely over the oozing surface from which adhesions have been separated, pressing the aristol upon these tissues firmly with a pad of gauze, and then leaving the area exposed to the air for a moment until the lymph-coagulum engages most of the aristol in its mesh. This presents a mechanical obstacle to the re-formation of adhesions. The author has found aristol in the tissues of animals after experimentation, several months after operation. This material probably disappears in time through slow liquefaction in the fat of cells which are undergoing retrograde metamorphosis.

To prevent the re-formation of peritoneal adhesions by using Cargile membrane, this material is laid upon oozing surfaces from which adhesions have been separated, and it may be caught at several points with strands of very fine catgut in case it does not adhere well enough naturally. Fingers and instruments must be very dry while applying this animal membrane; otherwise, it has a tendency to adhere to the fingers and instruments, rather than to the tissues of the patient. Cargile membrane is best transferred from a pad of dry gauze to the incised tissues. Animal membrane used in this way acts like the aristol film in presenting a mechanical obstacle to readhesion, but, unlike the aristol film, it has a tendency to undergo very rapid absorption in the peritoneal cavity, remaining sufficiently long, however, as a rule, to serve as a conductor for new endothelium beneath its protecting surface. Lubricating adhesion areas with sterile oil at the time of operation is favored by some surgeons, on the ground that per-

istalsis keeps oiled tissues moving too freely to allow of adhesions.

Adhesions for the most part undergo absorption by lymphatics under ordinary physiologic conditions, but where there has been much disturbance of tissue, infective or traumatic, the connective tissue which replaces the reparative lymph may remain permanently. It may act in various ways: by inhibiting peristalsis of the bowel and causing constipation, or exposing the patient to the danger of angulation of the bowel at adherent points. Adhesions may cause local irritation and discomfort only, or they may lead to complete strangulation of any of the tubular structures. They may become pulled out into long strands which ensnare the bowel, or which roll the omentum into abnormal positions, and they may prevent the normal gliding of viscera, and give rise to distant reflex disturbances.

In separating recently formed adhesions, it is best to separate them in as limited a way as will suffice for the completion of our work. The reason for this is because recently separated new adhesions are prone to re-form immediately in spite of all our efforts, and they may re-form in such a way as to be more injurious than when gradually arranged according to nature's plans.

To avoid the danger of formation of adhesions which were not present at the time of an operation we avoid rough handling of the peritoneum, which not only increases operative shock, but which stimulates the peritoneum to throw out an undue amount of lymph. The danger of the formation of such adhesions following traumatism produced by the operator

is sometimes greater than the danger from adhesions which form under local septic conditions.

When in the course of operative work it becomes necessary to withdraw loops of bowel, omentum, or other intra-abdominal structures, it is important to prevent them from becoming dry, chilled or exposed to the vast numbers of bacteria constantly falling upon them from the air, and this is obviated by covering exposed surfaces with a thin sheet of rubber dam or of gutta-percha tissue while we are at work. Gauze as a protective agent is objectionable, because it injures the endothelial surfaces at once unless it is quite wet with saline solution, and has a special tendency to cause subsequent adhesion formation.

Some peritoneums do not form adhesions of consequence, even under marked provocation, while in other cases they appear despite all precautions. Consequently in abdominal surgery we must always have in mind the possibility of adhesion formation which may nullify our best efforts in an operative way. Traumatism of the peritoneum is particularly to be avoided when we wish to sponge out fluids from the peritoneal cavity, and this sponging can often be done between the fingers of the operator's two hands. He places his hands about the field which is to be sponged in such a way as to make a little well down to the fluid, and the assistant, carrying gauze into the abdominal cavity, brushes the gauze repeatedly against the fingers of the operator, rather than against the delicate peritoneum.

The two points at which we need to open the peritoneal cavity most

often for relief of adhesions are in the bile-tract region and in the cecal region. The incision for reaching adhesions in the bile-tract region is commonly made along the free border of the ribs over the adhesion area, and in the cecal region the ordinary incision for reaching the appendix suffices.

Specially prepared membranes and other foreign bodies are useless for the prevention of adhesions. Thorough asepsis and all possible avoidance of trauma and exposure to air are the main desiderata. Sound methods of preventing or treating troublesome adhesions consist in covering denuded areas with peritoneum, suturing a part of the mesentery or omentum between the 2 surfaces, or holding the latter away from each other after the adhesions have been cut by shortening the normal supports of the organ or suturing it or its supports to some other peritoneal surface. In marked adhesion involving only a loop of intestine, the adhesion should be left alone and the bowel short-circuited above and below by a lateral anastomosis between the two limbs. R. C. Coffey (Jour. Amer. Med. Assoc., Nov. 29, 1913).

Many desperate adhesion cases can be greatly benefited by postural treatment after the adhesions have been broken up at operation. Report of a case in which before wound closure the abdomen was filled with saline solution. As soon as the patient reacted from the anesthetic she was placed in a sitting position, and kept at least partially upright until she left the hospital. She was still well 4 years later. This method requires that all or nearly all the adhesions be broken up, in order that the abdominal contents may sag as much as they are likely to immediately after the operation. Reichelderfer (Surg., Gyn. and Obstet., Dec., 1913).

Satisfactory results reported from the use of omental grafts to cover raw surfaces after separating adhesions between adherent coils. The free border of the omentum is used. No more tissue than is actually necessary should be removed, but the transplant should be large enough to cover the raw area and project beyond its margins on every side. The grafts are anchored with fine catgut sutures. L. Freeman (Annals of Surg., Jan., 1916).

In 400 celiotomies, to prevent adhesions, the writer used a solution of **sodium citrate** and **sodium chloride,** of each 2 parts, in water 100 parts; all the sponges and gauze pads were moistened with this solution. Saxton Pope (Annals of Surg., Feb., 1916).

Adhesions tend to disappear spontaneously if left alone. Infection seems to be the most important etiological factor; trauma intensifies its effect. Postural treatment is an important question in minimizing the symptoms of adhesions. Omental grafts may be used in covering raw surfaces, but never in the presence of infection. The use of sodium citrate or of oil does not seem to be justified. Foreign bodies, such as Cargile's membrane, in themselves produce adhesions. Hematomata are a cause of adhesions. The **cautery** is a useful preventive agent. Section of nerves, such as may occur in the right rectus incision, predisposes to adhesions. J. F. Corbett (Surg., Gynec. and Obstet., xxv, 166, 1917).

INTESTINAL SUTURES.—

Operations on the intestinal tract, despite their number and variety, can be reduced to a few simple steps of technique of which the most important element is the application of sutures and other retentive apparatus.

In excision the principal stage of the operation is with the insertion of sutures. In primary anastomoses the application of the suture constitutes most of the operation. The cutting, consisting of making a communicat-

ing opening after the suturing, is partly done. A general outline of suturing and its substitute procedures is therefore necessitated.

To secure union in most wounds of the bowel a continuous suture of fine catgut is first passed through both mucous and muscular coats, and the peritoneum is closed over all with a continuous Lembert suture of fine silk.

Silk or linen thread are necessary for all sutures of the bowel which are to hold more than a few hours, for the reason that catgut is digested very quickly, if it enters the secreting glands of the bowel, and it is commonly taken up also with great rapidity by the peritoneum. This two-plane suture known as the Czerny-Lembert is the evolution of years of intestinal surgery, and is so firm as to prevent any possibility of leakage, but the apposition of the two peritoneal surfaces insures peritoneal union almost immediately.

In most cases it is best to scarify the peritoneum with the point of a needle wherever peritoneal adhesion is desired. This scarification with the needle insures the exudation of a large amount of reparative lymph. Any narrowing of the intestinal caliber under this suture is for the most part temporary, as expansion of the bowel will take place at that point later, and even the loss of a third of its circumference does not lead to actual stenosis.

Any operation which consists in the closure of a wound in the long axis of the bowel involves in general no different suturing. This applies also to certain operations for pyloroplasty and gastroplasty when a transverse incision is changed into a vertical one with a resulting increase

of caliber. Whenever a cut surface of intestine does not enter into the restoration of continuity, it must be closed by a suture in the same way and under the same principle as linear wounds. Sutures of this type are applied to the cut surface of the stomach or intestine when these do not enter directly into anastomosis. In pylorectomy for cancer by Billroth's first method the cut stomach is simply sutured down to a point which makes the caliber the same as the caliber of the cut duodenum. A cut end of intestine may also be closed by Lembert sutures, for the principle remains always the same.

Peritoneal or mesenteric flaps are of substantial value for suture insufficiency in all abdominal operations. According to the writer, omental flaps, on the other hand, are not deserving of much attention. The first 2 can take the place of the Lembert seromuscular suture, the last cannot. A striking difference in the results has been observed by the writer. Sasaki (Deut. Zeitsch. f. Chir., cxiii, 62, 1913).

For the sterilization of ligatures and sutures which must remain within the wound, the writer uses, in preference to the method of Claudius, a solution made of iodine, 1 per cent., and iodide of potassium, 1.75 per cent. The whole of the iodine is thus taken up, a darker and stronger solution results, and catgut soaked in this for 10 days or more is almost black in color, and so strongly permeated by iodine that it is exceedingly difficult to infect it. Moynihan (Brit. Jour. of Surg., July, 1920).

When two cut surfaces are to be directly united by so-called end-to-end anastomosis the double plane of suture is applied as before, but the exigencies here are such that it is sometimes advisable to insert some

of the peritoneal sutures first. Thus the serous sutures are placed for about one-half the extent of the opening to be closed; then the deep penetrating layer is inserted for the entire circumference, and finally the balance of the serous sutures are inserted.

This plan of suturing is followed in a great variety of procedures, and as a rule for end-to-end anastomoses and implantations and secondary suturing in general. In primary anastomoses the principle is the same, some of the suturing being done in the interest of accurate coaptation before the anastomotic opening is made. Thus, the parts to be joined having been placed in juxtaposition, with the fingers or with clamps, the two portions of gut are first joined by a number of serous sutures, about half the number to be required eventually. The opening is then made and the all-embracing layer of continuous catgut serves to unite the edges of the same, after which the serous suture is completed.

> To prevent small masses of mucosa from pouting beyond the suture line while invaginating the mucosa by the ordinary methods of suture, the writer passes the suture from the mucosa outward through all the coats of the intestine, instead of from without in, as is usually done. V. Schmieden (Zentralbl. f. Chir., April 15, 1911).

McGraw Ligature. — A loop of bowel is brought against the portion of stomach with which it is to be connected, and the two structures are fastened together with a continuous durable Lembert suture for a distance of two and one-half inches. The stomach and bowel are then fastened together with a McGraw strand of solid rubber introduced with a large needle, preferably the Hagedorn full-curve type. The needle is passed

through the wall of the stomach to the lumen, and then brought out again at a point two inches away. The needle traverses the wall of the intestine in the same way. The rubber strand then being drawn tight is tied in such a way as to constrict the included parts as snugly as possible. The elastic-rubber knot is still further held by tying it with a strand of silk or linen. The next step completing the operation consists in approximating the portions of stomach and bowel which were left free after the preliminary suturing was done. The McGraw ligature was devised originally for gastroenterostomy, but is useful as well for enteroenterostomy.

Murphy's Button. — Wherever great speed in operating is a desideratum Murphy's button gives an advantage, and if it were not for the fact that buttons are sometimes retained, or that they sometimes give rise to complications *per se*, a very large part of our intestinal anastomosis work could be done with the aid of this ingenious resource.

Two-stage Operations. — Some of the procedures for establishing gastrostomy, enterostomy and colostomy are performed in two stages, the delay being for the purpose of allowing adhesions to form about the incisions and thereby protect the peritoneal cavity. Any operation whatever in which the external wound is not completely closed may become a two-stage procedure if a special operation is necessary to close the wound. As a rule, however, a considerable interval elapses in such cases, too long in fact to enable us to regard it as a single operative intervention. When wounds are closed outright there is a

possibility that they may at once require reopening for hemorrhage or sepsis. Hence, despite modern asepsis which has enabled us to operate so extensively in one stage, the abdominal operator is constantly exposed to the possibility of operating in successive stages.

SURGICAL DISEASES OF THE STOMACH.—We shall first enumerate the disorders in which surgical procedures are necessary, and then describe under a special heading the various operations resorted to.

Gastric and Duodenal Ulcers.—These require a variety of surgical procedures at various stages of their development. Recent or older ulcers may cause fatal hematemesis, perforative peritonitis, and crippling adhesions. From their location near the pylorus, actual or healed ulcers may cause pyloric stenosis. It must not be forgotten, however, that gastric and duodenal ulcer is a malady largely amenable to medical treatment, some forms not requiring surgery at all, but surgical intervention is indicated just as soon as medical resources lose efficiency, and at an earlier period than is customary as yet. The better diagnoses made by physicians in late years, and the extremely satisfactory surgery of the present day bring the question of time for operation to a point which can generally be agreed upon by expert physicians and surgeons.

Gastric ulcers are frequently multiple, and unless one is aware of this fact he may overlook others while caring for the first one which appears in the course of an operation. An active ulcer of the stomach may be surrounded by latent ulcers, or by scars which need excision, or which call for gastroenterostomy quite as much as the acute condition.

Perforating ulcer of the stomach is the one most often calling for immediate operation, while the chronic changes of the stomach due to scarring from old ulceration allow of more deliberate action.

The so-called bleeding ulcer without induration or tendency to perforation, while chiefly medical, sometimes calls for surgical relief, and it is sometimes very difficult to find the bleeding point; but, if the stomach is opened at a point not far from the pylorus, pressure of the finger upon various folds and rugæ or gentle wiping with a small gauze pad will excite hemorrhage anew. The arteries leading to this area may be ligated or separated, or, if the site is far enough away from the pylorus to avoid the danger of stenosis, a simple infolding of this part of the stomach wall with sutures results in putting this part of the stomach at rest out of the range of peristalsis, with a tendency to cure of the ulcer.

Even a chronic ulcer thrown out of the range of peristalsis by infolding of the stomach wall may sometimes go on to cure, but in the latter class of cases it is usually best to excise and to perform a gastroenterostomy. If the pancreas is involved in an operation for ulcer of the stomach, any escape of pancreatic secretion may cause local necrosis of tissues. Where the pyloric portion of the stomach is much scarred from old ulceration, or engaged in active ulceration, complete excision of this part of the stomach followed by some form of intestinal anastomosis is called for. Ulcer of the stomach at a distance from the pylorus causes some-

times hour-glass stomach through contraction of its scars, and the operation for this condition is referred to elsewhere.

Gastroenterostomy is a satisfactory operation in duodenal ulcer, especially if supplemented by Enriquez's sphincterectomy, which eliminates pylorospasm and establishes pyloric exclusion. In gastric ulcer the author for the last 8 years has been resecting, along with the ulcer, the pylorus and a variable additional mass of tissue. Such an operation alone gives complete and lasting results. Among 217 gastrectomies the mortality was nearly 10 per cent., but in some of these there had been grave hemorrhage, suppurative perigastritis, or involvement of the liver or pancreas. After the resection a posterior gastroenterostomy is added. Where neighboring organs have been eaten into by the ulcer the cavity is painted with iodine. In very weak patients, with the lesion near the pylorus, the operation is done in 2 stages—first a gastroenterostomy, and, 3 or 4 weeks later, the secondary gastrectomy. In spite of postoperative recovery of perfect digestive functions, the patient must continue to observe a careful dietary. Victor Pauchet (Bull. de l'Acad. de Méd., Dec. 18, 1917).

Among 863 cases of gastric ulcer dealt with at the Mayo Clinic, operative mortality was somewhat over 3 per cent., and 8 per cent. had gross hemorrhages after operation. The other symptoms were almost always completely relieved by **gastroenterostomy**, but not the bleeding. **Excision** combined with gastroenterostomy gave the desired protection against hemorrhage. The **actual cautery** is the safest and surest method of removing the ulcer in most instances. Balfour (Amer. Med. Assoc.; N. Y. Med. Jour., June 28, 1919).

From Jan. 1, 1906, to Jan. 1, 1920, 1191 patients were operated on in the Mayo Clinic for gastric ulcer, 4532 for duodenal ulcer, and in 203 ulcers were found in both regions.

Gastroenterostomy gives a high percentage of cure, but it should not be made without positive evidence of ulcer. Ulcer of the stomach may become malignant; ulcer of the duodenum does not. The operation preferred in the Clinic is **excision** or **cautery** destruction of ulcer of the stomach and destruction of all duodenal ulcers that cause hemorrhage. Gastrojejunal ulcers, while rare, may be avoided largely by the use of absorbable suture material. Sleeve **resection** is recommended in hour-glass contractions of the stomach from ulcer, with excision of the lower portion in the rare cases of recurrence. In extensive ulceration and thickening of the pyloric region resection of the involved lower third of the stomach with **anterior gastrojejunostomy** and end-to-side attachment is advised. C. H. Mayo (Trans. Miss. Valley Med. Assoc.; Med. Rec., Dec., 1920).

In gastric and duodenal ulcers **excision** remains the operation of choice, but it cannot always be the method chosen, much depending on the location of the ulcer, its size, the degree of involvement of the visceral coats, extent of induration, etc. It is the writer's practice, whenever possible, to excise the ulcer with the knife or cautery. When the ulcer has not to any great extent impaired the mechanism and the motility of the stomach, simple excision without a posterior gastroenterostomy will suffice. But from the standpoint of rationality and cure, *i.e.*, subsequent freedom from symptoms, gastroenterostomy is indicated in all cases that present marked hyperacidity before operation. J. B. Deaver (Surg., Gynec. and Obstet., Feb., 1921).

The average death rate for the 4-year period after operation in patients with gastric ulcers was found slightly more than 3 times the normal, while in patients with duodenal ulcers it was, if anything, less than normal. Gastric ulcers may give greater discomfort than duodenal ulcers, and because of the danger of malignant degenerations, they should be destroyed

at the time of the operation unless the procedure would add unwarranted immediate risk. While blocking the pylorus has been recommended in addition to gastroenterostomy, the procedure was unnecessary and is now obsolete. C. H. Mayo (Annals of Surg., Mar., 1921).

The author's record of operated cases of gastric ulcer since 1909 is given as follows: Gastrectomy, 96 cases, 2 deaths, or 2.08 per cent.; gastroenterostomy: posterior, 701; anterior, 8; in Y, 13; gastro-enterostomy in Y with jejunostomy, 14; gastroenterostomy in Y with gastrostomy, 2; total, 748 cases, 7 deaths, 0.9 per cent. Excision of gastric or duodenal ulcer with or without gastroenterostomy, including Balfour's operation, 43 cases, 1 death. Grand total of gastric and duodenal ulcers, 878, 10 deaths, or 1.11 per cent. J. B. Moynihan (Med. Rec., May 28, 1921).

The various resources for giving gastric and pyloric ulcer a chance to heal spontaneously without excision of the involved area would often be preferable, were it not for the fact that cancerous degeneration of the embryonic blind tubules at old ulcer sites is a frequent occurrence.

An inexperienced operator had better attempt a primary anastomosis perhaps and risk the cancer. Jejunostomy purely for artificial feeding may be done to prolong life in cases where the patient is unable to withstand a prolonged operation. When the surgeon is first summoned after perforation has occurred, it is not only necessary to expose and suture the opening and cleanse the peritoneum, but it is often advisable to take advantage of the opportunity for performing a radical operation, if one is actually indicated. This is also the case oftentimes in emergency intervention for hemorrhage from an ulcer, and in penetrating wounds of the stomach it is further necessary to cleanse the peritoneal cavity in the vicinity.

Carcinoma.—The most radical procedures are indicated only when there is some expectation of cure. With early recognition and improved technique the operative mortality is slowly diminishing, and operative procedures for comfort of the patient, rather than for cure within the three-year limit, are increasing in proportion. A preliminary laparotomy is often required to make a diagnosis of operability in cancer. It is often advisable to add a gastrotomy, as otherwise early malignant disease has been overlooked.

The only operation for radical cure is partial gastrectomy with extirpation of neighboring lymph-nodes. Since patients with well-recognized cancer of the stomach seldom live beyond a year and suffer greatly, palliative operations are indicated in theory, but it must be remembered that the mortality is rather high in such intervention. The resulting prolongation of life is also so slight that in ordinary cases the risk would hardly be worth while were it not for the considerable mitigation of suffering. When a palliative operation is undertaken, one with a minimum of intervention is indicated. Jejunostomy is satisfactory; it provides artificial alimentation and complete rest of the stomach. In certain cases a gastroenterostomy may be preferable.

Case of advanced gastric cancer in which an exploratory laparotomy materially improved conditions, though the neoplasm was too large for removal. Lenoir and Gardin (Arch. des Mal. de l'App. Digestif, June, 1917).

From 1897 to 1919, 2094 operations for cancer of the stomach were per-

formed at the Mayo Clinic. There were 736 resections with a mortality of 13.7 per cent.; 746 explorations, with 2.9 per cent.; and 612 palliative operations, 11.1 per cent. The common type of operation was the Mikulicz-Hartmann-Billroth No. 2, of which there were 359 with a mortality of 12.5 per cent. There were 19 of the Billroth No. 1 type with a 5 per cent. mortality, 28 sleeve resections and 7 Kocher operations with a mortality of 14.2 per cent. each, 115 posterior Polya operations, 14.7 per cent., and 120 anterior Polyas, 13.3 per cent. The local resections, 12 in number, gave the highest mortality, 25 per cent. For the last 3 years the anterior instead of the posterior Polya operation has been used. Better after-results seem to be obtained by turning the bowel to the right, closing the end of the stomach in toward the lesser curvature and protecting the closed portion by suturing the unopened bowel over it. During the 3 years previous to September, 1917, patients who recovered from the operation and were heard from numbered 306; 115 (37.6 per cent.) of these had 3-year cures. C. H. Mayo (Annals of Surg., lxx, 236, 1919).

The writer reports an operative death rate of 12 to 20 per cent. in his 300 gastrectomies for malignant tumors. The survivals have varied from 6 months to 9 years. He deems pessimism in regard to **gastrectomy** for cancer unjustified. With half of the stomach he removes a large part of the omentum, above and below, in a single piece. Before the operation the teeth are cleaned by a dentist, the gums painted with iodine morning and night, and the mouth rinsed with hydrogen dioxide. The nose is disinfected with an antiseptic oil, and the patient trained in deep breathing through the nose and accustomed to the semiseated position. The stomach is rinsed out several times during the preceding 2 days. If there is pyloric obstruction, he gives an alkaline water up to 2 or 3 liters (quarts) a day by the drop method, by the rec-

tum or by subcutaneous injection in the axillæ or under the mammæ. If haste is necessary, intravenous injections of 30 per cent. **glucose solution,** or, in case of acidosis, 30 per cent. **sodium bicarbonate solution** are given, with **epinephrin** and other stimulants as needed. He operates always under local, regional, or spinal anesthesia, and keeps up **gastric lavage** as long as there is vomiting, using hot saline. **Fluid** to 3 liters (quarts) a day must be supplied in some way, and **deep breathing** 5 or 6 times every hour is ordered. V. Pauchet (Jour. de Chir., xvi, 129, 1920).

Congenital Stenosis of Pylorus.— Patients with this affection, even when severe, have been known to recover under medical treatment, while operation for radical cure had, until recently, a high mortality, excepting at the hands of experts. Einhorn has devised an apparatus for dilating the constricted pylorus. If medical measures fail, pylorotomy or gastroenterostomy is indicated early.

The Webber-Rammstedt operation is less dangerous than the posterior gastroenterostomy, and produces more immediate relief. The abdomen is opened through the right rectus above the umbilicus. The tumor is delivered and while it is held firmly between the left thumb and forefinger, an incision is made into the tumor in the line of the axis of the gut, extending the full length of the swelling. This incision is carefully deepened until the mucous membrane begins to bulge into it. With scissors, the muscle is gently separated from the mucous membrane and the incision stretched open so that the membrane is exposed for a width of an inch or more. But little surgical shock results. Hypodermoclysis of 100 to 200 c.c of **normal saline** and 4 per cent. **glucose solution** should follow the operation; stimulation is provided by hypodermic injection of **adrenalin** in 5-minim (0.3 c.c.) doses;

external heat is applied; until the effect of the anesthetic is over the baby is kept with head downward, then placed semi-upright, to facilitate emptying the stomach and eructation of gas. An hour after operation, a few drams of water are given; an hour later, 3 drams (4 c.c.) of the mother's milk and 1 of water. This is repeated at 3-hour intervals. If possible, breast milk should be provided, and normal nursing resumed in a week or 10 days. Gallie and Robertson (Can. Med. Assoc. Jour., vii, 1, 1917).

About 200 cases seen by the writer convinced him that the treatment was operative. In 100 cases in which vomiting had not lasted over 4 weeks the mortality was 40 per cent., while in those in whom the vomiting had lasted over 4 weeks it was 50 per cent. This showed very clearly that the chances from operation are very much better if the operation was performed early. While the risk of operation is something to be considered, the risk of not operating is greater than the risk of operation. Hemorrhage occurred in very few cases. In his last 50 or 75 cases there had not been a serious complication. Food was given immediately after the child came out of the anesthetic, and the amount gradually increased until at the end of 48 hours it was getting 1 ounce of breast-milk at a feeding. At the end of a week the child was getting 2 ounces, but the child was never put on the breast pure until 9 or 10 days after the operation. The after treatment of these cases is much more difficult than the operation. L. Emmett Holt (Trans. Amer. Pediat. Soc.; N.Y. Med. Jour., Sept. 28, 1918).

In reporting 5 successful cases by the Rammstedt operation, the writers urge that breast milk must be given, feeding being begun 2 hours after the anesthesia has disappeared. They give 3 c.c. of breast milk and 3 c.c. of barley water, increasing gradually until 30 c.c. of breast-milk are given every 3 hours during the day and every 4 hours during the night. Breast nursing is only permitted 5 to 7 days after operation. Green and Sidbury (Surg., Gynec. and Obstet., Feb., 1919).

The writer regards as surgical all cases in which the symptoms indicate complete or incomplete obstruction of such a degree that not sufficient nourishment can pass to maintain nutritional balance. The symptoms are continuous depression of the weight curve, non-fecal or slightly fecal stools of small bulk, and continuous and severe propulsive vomiting. The surgical treatment is **posterior gastroenterostomy, Rammstedt's operation** and **Strauss' operation**. The latter has the simplicity of Rammstedt's method and also reconstructs the pyloric muscle.

The non-surgical cases are those in which sufficient nourishment passes to maintain the nutritional balance at least for a more or less extended period and those in which there is but slight loss in weight and it shows alternate losses and gains though its general trend is horizontal.

Medical treatment is usually directed to control the vomiting. Breast feeding or highly **alkalinized artificial food** should be given, with **stomach washing** once or twice a day with **warm bicarbonate of soda solution. Bromides** are all that medicinal treatment has to offer. H. Lowenburg (Penna. Med. Jour., xxii, 712, 1919).

Analysis of 163 cases in which the **Rammstedt operation** was performed. Of these, 131 children recovered and 32 died, a mortality of 19.63 per cent. In all cases except the 7 in which death was due to complications, the fatal result could definitely be attributed to a state of inanition existing at the time of operation. The mortality in artificially fed babies is more than 3 times that for the breast-fed babies. Goldbloom and Spence (Amer. Jour. Dis. of Children, Apr., 1920).

Early surgical treatment is indicated in all cases. **Rammstedt's operation** appears to be the only procedure which restores the pylorus to a condition approaching normal. The

general practitioner accustomed to surgical technic can successfully perform this operation, even in the most severe cases. MacDonald (Lancet, Feb. 26, 1921).

Hour-glass Stomach.—This condition is considered by some under the results of gastric ulcer, its usual causation. When it is discovered by exploratory laparotomy, or, better, with the fluoroscope, gastroplasty or gastrogastrostomy may be indicated, the former for enlarging the diameter of the constricted portion, and the latter for establishing a new communication between the stomach pouches when the first-named intervention is impracticable. Since some operators perform a secondary gastroenterostomy in such cases to avert the necessity for a possible second operation, it becomes a question whether a primary anastomosis is not the indication of choice. The latter in any case may be made with one or both stomach pouches, according to circumstances.

Gastroplasty is suitable only for cases in which the pouches are movable, their walls free from induration, and the constricted area narrow. Gastrostomy is especially adapted where the stomach is adherent along its lesser curvature to the liver, in which the pouches are relatively large, nearly equal in size, and can be approximated at their dependent portions. Mediogastric resection or resection in continuity is the ideal operation provided the pylorus is not stenosed, and should be performed in all suitable cases. Unfortunately, it is limited to the cases with few adhesions in which the pouches are fairly large, and permit of free mobilization. Midgastric resection performed by the author in 5 cases; in 3 a perfect result seemed to have been obtained, all symptoms having disappeared. W. A. Downes (Surg., Gynec. and Obstet., Jan., 1918).

Non-obstructive or Atonic Dilatation.—Atonic dilatation of the stomach or gastric myasthenia, like pylorospasm and relaxation of the pylorus, is only a symptom of something else which needs to be worked out before we consider any operative work, but when the patient is losing ground in spite of other treatment, and we have pyloric obstruction due to kinking, a gastrojejunostomy or Finney's operation will make the work of the physician easier. Finney's operation is preferable in cases in which the gastric motility is not much impaired. Gastric adhesions involving the stomach lessen the movements of the muscularis of the stomach, disturb circulation, and produce disturbances which predispose to ulceration, and a simple separation of these adhesions in some cases of chronic ulcer of the stomach or pylorospasm or relaxed pylorus obviates need of other treatment.

The operation of gastroplication, however, is usually performed for non-obstructive or atonic dilatation, with or without a secondary gastroenterostomy; but there are very many cases of atonic dilatation which do not properly belong to surgery at all, and we must look for these conditions as reflex from some peripheral irritation, or some central nervous derangement. Atonic dilatation may result from exhaustion of the muscularis due to persistent attempts for years at overcoming partial obstruction at the pylorus, due to the presence of adhesions or ulcer scars. It may be due to the influence of distant peripheral irritation, such as loose kidney or eye-strain, or to fibroid degeneration of the appendix.

All these possible factors must be very carefully excluded one by one, and all three are at the present day generally overlooked by diagnosti cians. Atonic dilatation occurring with certain psychoses, while belonging in the medical class, may nevertheless sometimes warrant surgical intervention.

Gastroptosis.—The operation of gastropexy or omentoplication for shortening the suspensory (gastrohepatic) ligaments of the stomach is indicated in this condition, if the gastroptosis occurs singly, but it is apt to be associated with panptosis, due to relaxation of peritoneal supports of intra-abdominal organs; so that at the same time we usually need to shorten the suspensory ligament of the liver, repair a diastasis of the rectus muscles, and perhaps fix loose kidneys in place. This severe operation makes it advisable to accomplish all that is possible with external supports before resorting to operative procedures. Most of the patients with visceral ptoses are neurasthenics, and surgery is of temporary avail only,—to-be avoided if possible.

Gastroplication, or shortening the lesser omentum, gives good results at first, but then the omentum stretches and the previous condition returns. Gastroenterostomy is absolutely contraindicated in gastroptosis. Gastropexy in 62 cases was applied by the writer, who reports 67.7 per cent. cured and 20.9 per cent. improved. Only 9.6 per cent. failed to derive benefit, aside from 1.6 per cent. who died. In 42 re-examined recently after over a year or more, only 4.1 per cent. were not improved or cured, outside of 2.6 per cent. who had died. In 6 cases he fastened the liver in place at the same time. When spasm of the pylorus was part of the clinical picture, he slit the pylorus lengthwise and sutured the lips together crosswise, with complete success in 11 cases.

In gastropexy Rovsing draws the stomach out through a median incision and makes an interrupted suture in the serosa, parallel to the lesser curvature, and reaching up close to the pylorus. Then, parallel to this, other rows of sutures are taken at intervals of 2 cm. The ends of the sutures are brought out through the abdominal wall to the left. The abdominal incision is then sutured and closed with collodion, and the ends of the suture material tied over a glass plate covered with gauze. The author's modification consists in carrying the suture material around the right costal arch or directly under it through the skin. The ends of the threads are brought out 4 to 3 cm. from their entering points and tied over glass drains wrapped in gauze. The stomach is fastened in its proper place and shortened in length at the same time. E. Bircher (Correspond.-blatt f. Schweizer Aerzte, Mar. 31, 1917).

Foreign Bodies.—Gastrotomy for the removal of foreign bodies is occasionally indicated, and does not differ from ordinary exploratory gastrotomy, excepting that the incision may be made very small in some cases, and just large enough to allow the entrance of forceps, which may be guided to the object through the aid of the fluoroscopic screen. This latter resource may also be used for reaching small objects in any part of the intestinal tract.

Stricture of the Esophagus.—Gastrostomy is required for some cases of stricture of the esophagus, to furnish access from two directions for dilatation purposes.

TYPICAL OPERATIONS UPON THE STOMACH.—Gastroplication. —This operation, which is intended

to reduce the size of the stomach by infolding its anterior wall, has been done successfully for simple non-obstructive dilatation, as well as for cases of pyloric obstruction due to the presence of bile-tract adhesions or ulcer scars. In several cases in which gastroplication seemed to be indicated because of dilatation secondary to the presence of adhesions, a simple separation of such adhesions, together with gastric lavage and massage subsequently, has allowed the stomach to regain its normal dimensions.

The principle of the operation involves the introduction of sutures placed within the seromuscular tissue. The more numerous and the longer the sutures, the greater the reduction in the capacity of the organ. The interrupted sutures are inserted at the lesser curvature, and passed in and out at intervals of one inch apart, until the anterior wall has been traversed without tying any sutures. They should be parallel in their course; the end sutures must not be placed so as to be in danger of constricting the lumina of the esophageal or pyloric orifices.

The sutures should be tied only when all have been placed in a row ready for knotting. If one suture were to be knotted in advance of, i.e., before, the introduction of the next one, it would run the operator along in an undesirable plane, for mechanical reasons evident while one is operating. The anterior wall will be puckered, creased or reefed according to the technique used, with resulting restoration of the natural capacity of the stomach. The sutures may be inserted in series of superimposed planes when the dilatation is excessive.

After gastroplication a cross-section of the organ shows a series of plaits if one plane of sutures is used; while, if several planes are superposed, a sort of diaphragm projects across the cavity. These formations tend to undergo some atrophy. Although the normal size of the organ is restored, the shape is not, and the tendency of the posterior wall to pouch must sometimes be offset by a posterior gastroenterostomy. It has even been counselled to perform the latter as a matter of routine.

A form of gastroplication has also been performed for gastric ulcer. The reef of the stomach wall which is the seat of the lesion is thus placed in relative rest, and under appropriate medical measures the ulcer may disappear during the atrophy. Two suture points usually suffice. Naturally the operation is best suited to ulcer of the anterior wall.

Gastric Omentoplication.—Gastric omentoplication may be mentioned in this connection. This operation consists in taking a tuck in the suspensory ligaments of the stomach, and is indicated in gastroptosis. These portions of the lesser omentum known respectively as the gastrohepatic and gastrosplenic ligaments are sutured in three superposed planes with mattress sutures, the deepest being inserted for a very short distance, one-half inch to one inch near the pylorus. The next plane projects well beyond the confines of the first, while the third corresponds to the amplitude of the tuck to be made. The sutures are then tied in the order of insertion. It must be borne in mind that the aim of omentoplication is to secure elevation without

compromising the mobility of the stomach.

Gastrotomy.—Incision of the stomach is indicated primarily for exploration of the stomach, and at the same time when required for the removal of foreign bodies, tumors, etc., checking hemorrhage, and dilating strictures at either orifice. It is always desirable after the laparotomy incision to examine the stomach thoroughly from without before incising its wall. The technique for incising the stomach is practically the same in different operations, although the site and extent may vary with the condition to be treated. The usual incision is made in the long diameter as far as possible from large blood-vessels, and is not less than three or more than five inches long. It is advisable to wash out the stomach before operation, but when this for any reason has not been done the organ must be evacuated by sponging gently with gauze or flushing with a siphon. Before incision the stomach must have been walled off from the peritoneal cavity with gauze. After the purpose of the operation has been fulfilled, the gastric incision is closed with one or more planes of continuous silk or linen sutures of the Lembert type.

When gastric ulcer is present some additions to the technique may be required. When the operation has been undertaken for hemorrhage from the ulcer, the latter must, if possible, be excised, and if an ulcer is found it is always best excised irrespective of the question of hemorrhage. It may, however, be impracticable to excise, from the position of the ulcer, or because of multiple ulcers or bleeding points, or the source of the hemorrhage may be obscure. Under such circumstances hemostatic procedures may be unavailable, and may even aggravate the state of affairs. The only resource in such cases is to perform gastrojejunostomy. Whenever an ulcer can be excised, the wound is closed first with catgut sutures, and a Lembert silk or linen serous suture must be superposed.

When the ulcer is seated on the posterior wall with implication of the serous coat, it can hardly be dealt with through the anterior incision, and therefore an incision must be made through the transverse mesocolon, and the posterior wall of the stomach brought into view. When the pylorus is the seat of the ulcer, simple excision will be inadvisable because of subsequent stenosis, and pyloroplasty will be indicated. When there is, besides, any evidence of esophageal stricture, great care should be taken to perform gastrostomy by a typical method, unless there is a possibility that the obstruction can be relieved and the treatment completed from above. It would be impracticable to turn an ordinary gastrotomy incision into a gastrostomy fistula.

Pyloroplasty (Heinecke - Mikulicz Operation).—This operation consists in restoring the original caliber of the pylorus when it is the seat of a simple stricture, or when suture following excision of an ulcer would result in pyloric stenosis. As cicatricial stricture of this orifice is due usually to the healing of ulcers, the operation is practically associated with this condition. Only a single procedure known as the Heinecke-Mikulicz operation is current in the narrower sense of the word, as other operations to which

the name is given are in part gastro-duodenostomies.

The technique is as follows: The stomach having been exposed by a median incision, the pylorus is drawn out, walled off from the peritoneal cavity, and incised. The presence of adhesions renders this stage difficult and sometimes furnishes a contra-indication. The incision may be made after an assistant has approximated the stomach and duodenum, each at a point some three inches beyond the stricture. The incision while made in the long axis of the pyloric end, extending from duodenum to stom-ach, is really made from following the pyloric curve, of a horseshoe shape. Any redundant tissue is ex-cised. If a fresh ulcer is present most authors prefer to do a gastroduo-denostomy. In order now to enlarge the pyloric lumen, forceps applied to the middle of each lip of the wound are made to pull it into a straight transverse incision. In this position it is sutured in two planes including the peritoneal layer, unusual care being required because the incision is not sutured in its original plane.

Despite the recommendations of Mikulicz and other eminent surgeons, the operation has many drawbacks. Adhesions are likely to result, and whether from this or other causes the stenosis may reappear. The indica-tions therefore are, as a rule, better carried out by performing some form of gastroduodenostomy or pylorec-tomy.

Pyloroplasty by Finney's (Gould's) Method and Gastroduodenostomy.—In both of these procedures an anas-tomosis is made between the stomach and duodenum, but the objects are entirely unlike, being in Finney's operation the widening of a stenosed pyloric orifice, while in the latter the pylorus is excluded outright by a short circuit. Gastroduodenostomy does not differ essentially from gas-troenterostomy in general save that the duodenum must be mobilized beforehand. As that step is also required in Finney's pyloroplasty, the latter alone needs a detailed descrip-tion.

The operative success will be due to the mobility of the duodenum, which may be and usually is more or less immobilized by secondary adhe-sions, and to such extent sometimes as to appear inoperable. Aside from adhesions the anatomic relations may be such as to require considerable operative manipulation to make the parts accessible, sometimes division of gastric ligaments. Traction sutures may then be inserted outside of the area to be incised for the purpose of steadying and tightening the tissue, but here it is better to use clamps, as in Gould's modified operation, which brings pyloroplasty in the same class as other anastomoses. The clamps grasp the duodenum and stomach in the long diameter—not in the trans-verse diameter, which would be the case in an exclusion of short-circuit anastomosis—with one clamp secur-ing the duodenum and the other the stomach just above the greater curvature; the two are brought side by side and the two portions of intestine united by continuous sero-muscular sutures. A U-shaped inci-sion is now made, the bend of which corresponds to the pylorus. Redundant mucous membrane is clipped off; the resulting diaphragm or tongue is overcast with a second row of continuous sutures, simple

communication now being established between the duodenum and stomach at the natural orifice. An elliptic space remains to be closed with two planes of sutures, one all-embracing and the other serous and muscular.

Gastrostomy.—*Hacker's Operation.* —This procedure is rather a small gastrotomy left unsutured than a true gastrostomy, in the modern sense of the term. It is recommended chiefly in emergencies. The stomach having been exposed and temporary traction sutures passed through its wall to steady the organ, two planes of permanent sutures are inserted on either edge of the wound. The first plane passes through the abdominal wall only, including the peritoneum; the second, placed just within the others, includes in its grasp the walls of the stomach, but without entering the cavity. The sutures are then tied and cut close, so that the stomach is fixed to the abdominal wall. Additional smaller sutures are left in place, and the wound packed with gauze.

At a subsequent period, usually the following day or the second day, the wall of the stomach is opened with a knife, the wound being one-half inch long or just the size to contain a tube which should fit closely. The traction sutures should now be withdrawn. The abdominal incision for this operation should be three inches long and vertical in direction, slightly over an inch to the left of the linea alba, and beginning about one inch beneath the costal arch. When the rectus muscle is exposed the anterior fascia is divided with the scissors, but the belly of the muscle is separated bluntly. The posterior layer of the sheath is again divided with the scissors, exposing the peritoneum. This is opened only sufficiently to admit the finger, but subsequently prolonged with blunt scissors, and the peritoneum and muscle sutured with catgut.

Franck's operation is a so-called valve operation, in which the portion of stomach wall to be incised is passed out of a relatively large orifice under a bridge of skin, and finally out of a smaller incision, in which locality it is incised.

The layer incision is known as Fenger's and runs parallel to the costal arch and about one inch below the latter, starting to the left of the ensiform cartilage and not exceeding two inches in length. When the parietal peritoneum is divided it is sutured to the muscles of the abdominal wall. With two fingers in this opening the anterior wall of the stomach is drawn out and the apex of the resulting cone transfixed with a traction suture, while a running silk suture unites the base of the cone to the edges of the wound, all the tissues being embraced except the skin and the gastric mucosa.

The lesser incision is parallel to the first and seated an inch above the margin of the costal arch. Its length should not exceed one inch. The tissues between the two incisions are then detached from the subcutaneous structures, when with the aid of the traction suture the apex of the cone is drawn under the bridge of skin and out of the lesser opening, to the edges of which it is sutured. The major orifice is then closed and the apex of the stomach cone opened, a tube being placed within the canal. The Fenger incision may be replaced by a vertical one, as advised by Robson and others.

Witzel's Operation. — The canal, which acts as a valve, passes obliquely through the wall of the stomach. The anterior surface of the latter is exposed in the usual manner and sutured to the wound; an opening is then made in the central portion, toward the greater curvature. Into this a soft catheter is passed; the portion outside the stomach is laid flat against the latter, and directed downward and outward.

Sutures are now passed through the seromuscular coats of the stomach over the tube and through the opposite side so that when tightened the tube is covered by a fold of stomach wall. The first suture point is seated one inch from the opening in the stomach and the entire length of the canal should be about an inch and a half. The abdominal wound is closed down on the free end of the tube, which is left projecting.

Kader's Operation. — The tube enters the stomach directly instead of obliquely, and the canal is formed by producing an artificial thickening of the stomach with certain planes of suturing. Thus with the tube *in situ,* two folds of stomach wall are formed by inserting sutures twice through the wall—one to each side of the tube. These are tightened and cut close, and similar sutures are next inserted just outside the first. Each plane comprises four sutures. The canal thus produced is about half an inch long and has a good valvular action.

A similar canal may be produced by several planes of purse-string sutures, as recommended by the late Dr. Senn.

Author's Operation. — The author constructs a fistula lined with epithelium, by utilizing long skin flaps. At the left costal border, over the chosen stomach region, make an incision five inches long through the skin and subcutaneous tissues directly cephalad from the costal border. Make a similar incision on either side of the first incision, giving two ribbons of skin each one inch in width. A transverse incision at the cephalad end of the parallel incisions frees the ends of the skin ribbons. The skin ribbons are next freed throughout their length, but remain attached at the costal border. The epithelial surfaces of the skin ribbons are placed in apposition and a running suture of catgut unites their margins. This transforms the ribbons into a tube of skin. The stomach is exposed and opened. The free end of skin tube is sutured with silk to the mucosa of the stomach. A rubber tube is passed through the skin tube. One end of the rubber tube is to remain in the lumen of the stomach until repair of the wound is complete. The other end of the rubber tube emerges from the skin tube on the abdominal wall, and serves for introducing nourishment. When the skin tube with its contained rubber tube follows the stomach into place, the remaining structures to be sutured have fallen together in such a way that the character of final suturing is apparent, and needs no description. After repair of the wound is sufficient, at the end of a few days, the rubber tube is removed. This leaves a fistula lined with epithelium extending between abdominal skin and stomach mucosa. The stomach has drawn the skin tube into position at such an angle that atmospheric pressure keeps the skin tube closed, excepting at times when food is to be introduced.

Gastrorrhaphy.—The operation comprises working beyond an emergency suture of the stomach wall for traumatisms, the latter including perforation from gastric ulcer. But since gastrorrhaphy is involved in suturing a gastrotomy wound there is little to be said under a special heading beyond the statement that some modifications arise from the nature of the injury. The technique of closing stomach wounds is described with gastrotomy.

> Description of a method of performing gastrostomy which prevents discharge of food from the stomach through the opening. Through a median incision the anterior wall of the stomach is seized near the cardia. The resulting cone is drawn through a tunnel made for it in a narrow strip of the rectus muscle, to the right of the median incision. The cone is then drawn farther toward the right, through a second tunnel 2 cm. beyond the first, the whole slanting upward and outward, and the tip of the cone is fastened in the upper portion of the last one of the three incisions in the skin. The stomach is fastened to the rectus muscle close to the first incision, and also to the strips of rectus muscles bridging it as the cone is drawn up toward the right to hold the whole in place. The protruding cone can be opened at once or later; the two small incisions are sutured at once. There is no danger of the sphincter thus made becoming displaced or twisted, and the fistula is continent in all positions. Solid food, finely chopped, can be given almost from the first. D'Agostino (Arch. ital. di Chir., iii, 285, 1921).

Gastroplasty.—Gastroplasty is a procedure which is indicated only in hour-glass stomach, and differs but slightly from pyloroplasty, the constriction of the organ taking the place of the pylorus. As in Finney's pyloroplasty, the two portions of the stomach are first brought together by sutures or clamps and a horseshoe incision made around the suture line at a distance of one-fourth inch. The inner or posterior edge of the wound having been stitched by a continuous suture, the outer or anterior edge is similarly treated. The communication between the two halves of the stomach is thereby greatly amplified. Re-enforcing sutures will probably be required for the anterior sutures.

Gastroplasty may also be performed along the lines laid down for the Heinecke-Mikulicz pyloroplasty, in which a transverse incision is changed to a vertical one. The value of the operation is in question.

> The writer carried out the following experiments in dogs: He implanted a section of the small intestine in place of resected pylorus. The fluoroscopic examination proved the absolutely good function of the implanted intestine and the examination of the specimen of the dog killed after weeks showed remarkable changes in epithelial structure, the epithelium of the jejunum growing similar to that of the stomach. C. Beck (Surg., Gynec. and Obstet., Feb., 1915).

Castrogastrostomy.—Like gastroplasty the operation is indicated only in hour-glass stomach. It consists of a simple anastomosis between the halves of the stomach, which then possesses two distinct communicating passages. The two stomach pouches are sutured together with a continuous Lembert silk suture along one side. The two pouches are next incised, and the cut surfaces joined as in gastroenterostomy, and final suturing completes the apposition of the pouches.

Partial Gastrectomy.—Partial gastrectomy, the name of which is self-

explanatory, is undertaken chiefly for cancer of the pylorus, and to a certain extent for cancer of the stomach proper, gastric ulcer, and hour-glass stomach. When performed for benign ulceration the cases selected are those near the pylorus when the lesion is unusually large, indurated or multiple. When done for hour-glass stomach the constriction between the stomach pouches is the seat of an ulcer, and the excision can be combined with gastrogastrostomy.

Technically the mere excision of a bleeding ulcer anywhere in the stomach is a partial gastrectomy, but in the typical operation the pylorus must be sacrificed, and therefore the continuity of the digestive tube must be restored by some form of gastro-enterostomy, either gastroduodenostomy by end-to-end anastomosis, a gastroduodenostomy by implanting the duodenum in the stomach wall, or an ordinary gastroenterostomy. Partial gastrectomy has been divided into a typical and a cylindrical method, but the former, which relates only to excision of ulcer areas in the stomach proper, is sufficiently comprehended under gastrotomy. Cylindrical gastrotomy is also termed pylorectomy, since the pylorus is always excised completely, alone or with more or less of the entire continuous gastric wall. Over a third of the organ may thus be sacrificed.

Billroth's Operation.—The original method practised by this surgeon was to excise the pylorus and the necessary portion of the stomach wall, and to suture the cut end of the stomach until it reached the size of the duodenum. The two cut ends were then joined by end-to-end anastomosis. At a later period the same surgeon preferred to close up both cut ends and perform a posterior gastrojejunostomy.

Billroth prefaced his pylorotomy by ligating the vessels of the greater and lesser curvatures, and next tied off the peritoneal attachments (gastrohepatic and gastrocolic ligaments). This mobilization enables the pylorus to be drawn out of the external incision. Clamps are then applied to either side of the pylorus, two pairs each to duodenum and stomach, at a distance of an inch from the diseased area. Fingers or clamps may be used on the proximal sides. The stomach and then the duodenum are divided between the clamps. The divided end of the stomach is sutured, after complete hemostasis is secured with a running suture of chromicized gut, passed through-and-through on each side in order to secure some inversion. The suture is carried from above downward to such a distance that the unstitched portion corresponds in size to the cut surface of the duodenum. A second through-and-through suture plane is added and serves to further invert the wound edges.

The duodenum is not divided until the stomach has been sutured. The two divided ends are now partly joined by a continuous Lembert suture, leaving room to apply an infolding through-and-through suture of chromicized catgut within the plane of the outside suture, which latter is then completed.

Kocher's Operation.—In this method the cut end of the stomach is completely closed while the cut end of the duodenum is implanted into the posterior wall of the stomach. The pylorectomy itself does not differ

'essentially from that of Billroth. The divided end of the stomach is completely closed by two planes of sutures, an inner continuous through-and-through suture of chromicized gut, and a Lembert suture outside of it. The essential part of the operation consists in the gastroduodenostomy by which the cut edge of the duodenum is implanted about two inches behind the closed wound of the stomach. The duodenum held in position with fingers is first made fast to the stomach by a running Lembert suture inserted at the point of contact with the stomach and occupying one-half of the gut just back of the cut edge. The stomach is then incised just beyond this suture line in such manner that the two edges may be exactly approximated. The anastomosis is now made with a continuous interior suture of chromicized gut, and the original outside suture is completed. The interior anastomosis suture is inserted by the through-and-through method, and traverses all the coats of the intestine.

Hartmann's operation differs from the preceding in that it includes extirpation of the lymph-nodes which are seated within the gastrohepatic ligament. It is therefore only applicable to cancer of the pylorus in a more or less advanced but still operable stage. The operation proper and its termination by gastroduodenostomy or gastroenterostomy are not different materially from the preceding.

Mayo's operation is also a radical procedure, and involves not only extirpation of lymphatics draining the pyloric area, but an unusual degree of removal of stomach, including all the lesser curvature. The stomach is closed entirely, and continuity restored by any of the methods in vogue.

Review of 266 partial gastrectomies involving the pyloric end of the stomach performed in the Saint Mary's Hospital, Rochester, between April 21, 1897, and Jan. 27, 1910. There were 34 deaths from the operation, a mortality of 12.4 per cent. Some of the patients are still living eight years after the operation. The writer does not believe the pessimism as regards this operation to be justified by the facts. He calls attention to two important indications for operation in gastric cancer: 1. Food remnants found repeatedly in the stomach after twelve hours should, when taken in connection with the clinical history, call for a surgical consultation, which in a large majority of cases will lead to an exploratory operation. 2. The finding of a movable tumor in the pyloric end of the stomach cannot be overestimated as to its surgical significance. Gastric cancer by itself does not give, he is convinced, characteristic symptoms during the curable stage. But if it is situated in the pyloric end of the stomach mechanical conditions are early induced which afford most valuable information. An effort should always be made to remove the lymphatic area, whether diseased or not. It must be removed before the lymphatics are infected. Prophylaxis of gastric cancer can be aided by the excision of calloused gastric ulcers, which are its origin in 70 per cent. A typical resection necessitates the removal of all that part of the stomach lying to the right of a line dropped vertically from the cardiac orifice, though in some cases more of the fundus must be removed on account of the direct extension of the disease. As a general rule, it will be most convenient to make the separation of the superior border of the stomach first, beginning the operation by (*a*) ligation of the superior pyloric vessel, (*b*) the gastric, (*c*) the left gastroepiploic, (*d*)

the gastroduodenal vessels. As each vessel is secured, the glandular separation is effected. In doing the anterior gastrojejunostomy he usually follows the method of Hartmann, *i.e.,* the two-row suture method with slight modifications. Generally speaking, the Kocher method of joining the jejunum to the stomach is not so satisfactory as the Billroth No. 2 method, *i.e.,* closing both the end of the duodenum and the stomach and making an independent gastrojejunostomy. When the patient is in good condition the operation has an operative mortality of under 5 per cent. In advanced cases, the resection is worth the risk, considering the short lease of life of patients left without it. W. J. Mayo (Jour. Amer. Med. Assoc., May 14, 1910).

In the method of gastrectomy described by the writer, a crushing instrument consisting of 3 sets of blades is used. The crushed tissue is cut across. An over-and-over suture is used; after removal of the proximal crusher an invaginating suture, beginning at the center and working out to the ends, is inserted. The distal portion of the stomach is raised with one section of crusher on the cut end. The duodenum is sectioned in one of several ways. A gastro-enterostomy is finally done in the usual manner. T. De Martel (Amer. Jour. Surg., xxxv, 227, 1921).

Complete Gastrectomy.—This operation, including subtotal gastrectomy, is now practicable as a method, and has radically cured perhaps a very few individuals of cancer, but is seldom attempted, the operative mortality being very great and cases suitable for such intervention seldom recognized in time. Removal of the stomach is not a difficult operation at all, but search for and removal of lymph-nodes must be very thorough. The removal is followed by an end-to-end anastomosis made between the duodenum and esophagus, or the cut end of the former may ᵣ closed and the esophagus implanted into the jejunum. The author has found it much easier to do the work if a small part of the cardiac end of the stomach is allowed to remain.

SURGICAL DISEASES OF THE PERITONEUM.—Septic Peritonitis.—This condition being in the great majority of cases secondary to some suppurative process either within or without the peritoneal cavity, the treatment cannot be considered independently of that of the primary condition, which consists fundamentally of incision and drainage of or removal of the pyogenic focus. The conditions likely to give rise to peritonitis are separately mentioned. If the focus is outside the peritoneal cavity, the latter need not necessarily be opened, because the peritoneum rapidly guards itself by hyperleucocytosis after a focus of infection is cared for. If the focus is in the peritoneal cavity, it may or may not be advisable to treat the peritoneum actively. If the peritonitis comes from an intestinal perforation an enterorrhaphy may be required, but it is often safer to make temporary drainage, and fistulæ following have a tendency to close spontaneously. Other cases may require excision, as when a portion of the gut is gangrenous. In many cases, however, posture and drainage alone are indicated, and any unnecessary handling of the peritoneum is to be deprecated. Only when drainage cannot offer a prospect of self-limitation of the process is a thorough cleansing of the peritoneum indicated, and this is best accomplished by flushing with **hot saline solution** through short incision, and the glass tube.

The mortality from peritonitis has been much reduced by Murphy's treatment, which consists in making a small opening in the abdomen, doing such operation at the point of origin of the peritonitis as is required, the introduction of a large drainage-tube into the pelvis, placing the patient in a sitting posture of 35 to 40 degrees, and the administration of **salt solution** every two hours by rectum. An important feature is to avoid handling the intestines or peritoneum more than is absolutely necessary.

It was Murphy's protest against general irrigation of the abdomen, showing that the higher mortality rested with those who used it, that first attracted the attention of surgeons to R. E. Kelly. His first paper dealt with 5 cases (including 1 typhoid case) without a death, was followed in October, 1906, with 28 cases with 1 death, and up to a later paper included 48 consecutive cases with only 2 deaths. These are astounding results when compared with the prior 50 per cent. mortality at the Mayo clinic.

The principles laid down by Murphy were: 1. Operate early. 2. Operate quickly. Murphy gave ten minutes as the average time in which to close the gastric or duodenal opening, or to remove the offending appendix or tubes. 3. The anesthetic must always be ether, if the patient can stand it; if not, then a local anesthetic. Stiles's work has shown how dangerous chloroform is in acute suppurative conditions, in the production and retention of acetone. 4. It is a fatal mistake to mop, wash, or handle the intestine. The peritoneum is essentially an absorbing surface; carmine granules injected into its cavity are rapidly absorbed especially in its upper half, and conveyed by the lymph-stream to the general circulation. Organisms similarly do harm by the rapid absorption of their toxins in a similar manner. Lymph is protective, and tends to prevent this absorption. 5. The Fowler position and a suprapubic drain. The object of the Fowler position is to allow the discharges to gravitate toward the pelvis, and away from the danger zone of the diaphragm. The patient, as soon as he has recovered from the anesthetic, is placed in the sitting posture, so that the abdominal cavity is vertical in position, and drainage is instituted by placing a large drain in the pelvis through a stab wound above the pubis. This drainage-tube is three-fourths to one inch in diameter, about eight inches long, glass, and goes down to the pouch of Douglas in the female, and the rectovesical in the male. In this position the tube is almost horizontal; and if it is filled with fluid, each excursion of the diaphragm will pump a small quantity of it out into the dressings. The hole is now at the most dependent part of the abdominal cavity. 6.
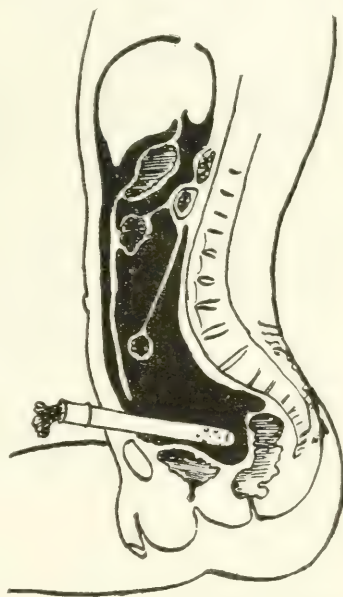
Peritonitis treated by the Murphy method

Proctoclysis or the absorption of large quantities of saline by the rectum for the first two days after operation. As soon as possible after the operation, a tube having numerous holes in it and one-half inch in diameter is inserted into the rectum for about two to three inches. This is connected by means of a rubber tube of the same diameter with a container suspended from four to twelve inches above the plane of the patient's couch, and the whole is filled with warm saline. By means of this head of water (it need only be four to six inches in height, as a rule) saline gradually trickles into the rectum at about the rate of three-quarters to one pint an hour. The temperature of the saline is kept at $100°$ F.

and should never reach 106° F., or it will not be retained. Editors.

Description of a scheme of treatment for peritonitis based on experience in 13,145 laparotomies. By this plan the mortality in all abdominal operations was decreased 33⅓ per cent., and in acute appendicitis alone, 67.6 per cent.: (1) **Nitrous oxide-oxygen anesthesia.** (2) Local anesthesia at site of incision. (3) Accurate, clean-cut operation to diminish both infection and shock. (4) Adequate drainage. (5) **Fowler's position.** (6) Vast **hot packs** over the entire abdomen, spreading well down over the sides. (7) Five per cent. **sodium bicarbonate** with 5 per cent. **glucose by rectal drip,** continued as long as it is tolerated. (8) Primary **lavage of the stomach,** repeated only if indicated. (9) From 2500 to 3000 c.c. (5 to 6 pints) of **physiological sodium chloride solution** subcutaneously every 24 hours until the period of danger is past. (10) **Morphine** hypodermically until the respiratory rate is reduced to from 10 to 14 per minute, and held to this rate until danger is past. The morphine is not useful in a streptococcus peritonitis. G. W. Crile (Jour. Amer. Med. Assoc., Nov. 29, 1919).

According to the writer, advancing postabortal peritonitis has a definite symptom complex in the presence of which **drainage** is necessary and definitely lowers the mortality. The patient is placed in the **high Fowler position;** one or more **icebags** are applied to the **abdomen,** and a **proctoclysis** by the Harris method of **glucose-sodium-bicarbonate solution** is begun. The pain is relieved by routine **morphinization,** small doses being given hypodermically at regular intervals. If the patient's resistance is capable of taking care of the peritoneal invasion, in from 12 to 20 hours there will be a definite recession in the severity of the symptoms and a fall in the polymorphonuclear percentage. On the other hand, if resistance is insufficient, or virulence greater than the protective reaction,

the pulse, temperature and local abdominal symptoms will remain stationary or increase in severity, and the polymorphonuclear percentage will rise. A **posterior vaginal incision** through the fornix will usually liberate a pint or more of thin, flocculent blood-stained serum which on culture returns innumerable streptococci. Polak (Amer. Jour. Obstet., Oct., 1920).

Report of 22 cases of peritonitis treated by **instillations of ether,** with 17 recoveries and 5 deaths. Of the former, 9 were in a very desperate condition when operated. The author believes himself justified in recommending ether treatment. Neudoerfer (Zentralbl. f. Chir., xlviii, 2, 1921).

Twenty-two cases collected from literature, among which **enterostomy** seemed to be the decisive factor in the recovery in 12 cases. A cone of intestine is drawn up, its base sutured to the skin, and a thread run around it about 2 cm. from the tip. A catheter is then worked into a minute opening in the tip and the thread drawn tight, fastening the tip of the cone to the catheter. The latter is then pushed in as far as desired, thus invaginating the cone and protecting the portion of the intestine fastened to the wall from any contact with the bowel contents. Aievoli (Riforma Medica, Apr. 16, 1921).

He who operates in a case of acute diffusing peritonitis after the first 36 or 48 hours of the onset of peritoneal inflammation, with no evidence of a localizing point, is, in the majority of cases, not serving the best interests of the patient. In the presence of a circumscribed peritonitis with a definite localizing point of exquisite tenderness, due to an acutely inflamed, perforating or gangrenous appendix, operation can be undertaken in the absence of constitutional or other contraindications, provided the proper technique is observed in safeguarding the peritoneum from contamination by the proper disposition of gauze packings. Peritonitis the result of intestinal obstruction, gas-

tric, duodenal, gallbladder, intestinal, or colonic perforation, should be immediately operated if the condition can be recognized, which it usually can if the case is seen early. Too thorough operation in peritonitis too often spells death. In peritonitis it is not the inflammation of the peritoneum that is fatal, but the toxins absorbed. J. B. Deaver (Trans. Phila. Co. Med. Soc.; Med. Rec., Apr. 30, 1921).

Tuberculous Peritonitis.—In theory the local focus of disease which has caused an extension of the process to the peritoneum should be excised, whether this is in the intestine, Fallopian tube, appendix, or other removable tissues. But this is not always practicable, and, furthermore, patients often recover under simple laparotomy and drainage. The author in a series of experiments with animals some years ago came to the conclusion that this cure of tuberculosis of the peritoneum after opening the peritoneal cavity was due to the presence of toxins developed from bacteria which grew in the culture medium of peritoneal exudate exposed by way of the drainage-tube. This was in fact true, and the cultures of tubercle bacilli in test-tubes were instantly killed by toxins extracted from such fluid and applied to the cultures. A later theory, however, and one which is borne out by later studies, is that the tubercle bacilli are destroyed by phagocytes in the course of the intense hyperleucocytosis which promptly follows opening of the peritoneal cavity for any purpose. The idea that such hyperleucocytosis proves destructive to the tubercle bacilli is further substantiated by the fact that various substances injected into the peritoneal cavity have proved effective in the same way, and for the destruction of tubercle bacilli in the peritoneum it apparently matters little which method for exciting exaggerated hyperleucocytosis is chosen, so long as we bring about that phenomenon.

According to A. K. Stone, operation should only be undertaken when there is some distress from the distention; it is better to wait for a period with the patient at rest and under the same hygienic conditions to which any case of pulmonary tuberculosis would naturally be subjected, namely, rest, fresh air, good food, and, later, moderate regulated exercise. If after six or eight weeks there is no improvement in the symptoms, operation should be considered. When once the disease is arrested, whether by operation or hygienic methods of treatment, the patients must be taught to regulate their lives with the same care that they would had their disease been located in the lungs.

Laparotomy alone should not be considered a cure, but the disease treated in the light of the pathological conditions found in each case. Often, when diagnosed early, the peritonitis is found to be confined to the region of the primary focus, such as the appendix, cecum, and Fallopian tubes. In such cases removal of the entire infected area with its underlying organ or organs is the rational method of treatment, to be followed by energetic hygienic measures and the administration of **tuberculin**. Where the disease has become so widespread that it cannot be removed surgically, laparotomy is not only not indicated, but may hasten the fatal issue. O. M. Shere (Colo. Med., June, 1917).

Surgeons are still in disagreement as to the operative procedure to be followed, whether simple puncture, simple laparotomy or laparotomy with consecutive peritoneal lavage. Cecherelli attributes vast importance to **lavage**. According to the author, it may be used in every anatomic variety of tuberculous peritonitis, and is absolutely indicated in the forms in which purulent diffused or circum-

scribed collections accumulate toxic material. Operation is probably indicated in all forms except where the tuberculosis involves the lungs or is spread to many viscera or where the general state does not permit it. Ruffo (Riforma Med., June 16, 1917).

The writer reports cure in 12 out of 15 cases and material improvement of the others by operative treatment. Through a median laparotomy he paints the whole accessible peritoneal surface with official tincture of iodine, loosening up adhesions only as necessary to reach all the surface. The abdominal wall is always sutured at once. Stocker (Corresp.-Blatt f. schweizer Aerzte, June 23, 1917).

Disappearance of effusion, when present, may be hastened by moderate purgation, diet restriction, and ordinary diuretics. X-ray treatment has benefited some patients. Laparotomy is indicated in serous effusion if, after several weeks of conservative treatment, satisfactory progress has not been made. Nitrous oxide oxygen anesthesia should always be used. C. A. Vance (Trans. Ky. State Med. Assoc.; Jour. Amer. Med. Assoc., Nov. 1, 1919).

In intestinal occlusion due to peritoneal tuberculosis, both the occlusion and the peritonitis may be treated by a laparotomy. An artificial anus is necessary only if the patient's condition is very poor or if it becomes evident that nothing else can be done. Aimes (Rev. de chir., lviii, 177, 1920).

The writer deems tuberculous peritonitis very amenable to cure in most instances, at least if the abdominal condition is the main factor. Nature can cure tuberculous peritonitis in pure form.

Mixed infection destroys tissue, but added toxins are destructive to life as well as to tissue, and are more chronic and difficult to treat or control. If ascites in tuberculous peritonitis adds so enormously to the surface area involved in a tuberculous process and must be overcome by changes in the peritoneum by chang-

ing the exudate from serous to fibrinous and plastic adhesions before cure occurs, such surgical treatment as will hasten the process is advisable. Death or even ill health rarely comes from obstruction due to the adhesions. When acute obstruction develops it is due to a single band or the hyperplastic variety without ascites.

By removing the focus of disease in tuberculous peritonitis, especially when such a focus involves a tuberculous mucous membrane, a high percentage of permanency of cure with a very low primary operative mortality is secured. Mayo (Minn. Med., Apr., 1921).

Ascites.—We speak of surgical treatment of ascites rather than of cirrhosis of the liver in cases of the latter disease, because the operation has probably little influence upon the liver itself. Ascites and hydroperitoneum from whatever cause may be relieved temporarily by paracentesis.

The incidental laparotomy with drainage corrects the condition for the time being. We have to be particularly careful to guard the peritoneum against infection in many of these cases, for the reason that the current of lymph is outward from the peritoneum, and it becomes exposed to various bacteria. When the current is inward, as in normal conditions, there is destruction of entering bacteria by the action of blood- and body- cells.

Warning against removal of recent tuberculous effusions. All patients operated on for tuberculous peritonitis within 2 months of its apparent onset have died, in the author's experience with 100 cases.. Only effusions from 3 to 5 months old should be removed. There follows spontaneously a new, curative effusion. This is the view now held by many clinicians. Gelpke (Corre-

Congenital Cysts of the Mesentery. (*H. C. Deaver.*)
Annals of Surgery.

spond.-Blatt f. schweizer Aerzte, Jan. 12, 1918).

Omentopexy or the *Talma-Drummond operation* has for its aim the establishment of adhesions between the omentum and parietal peritoneum. These adhesions become filled with capillary blood-vessels in time, and the free network of small new vessels constitutes a venous anastomosis around the area of obstructed circulation. This work may be done by introducing numerous pinpoint sutures, or by pulling the omentum between the transversalis fascia and the posterior sheath of the rectus muscle, and fixing it there.

In addition to establishing a new circulation by the roundabout way of adhesions of the omentum, it is well to scarify the cephalad surface of the liver and the corresponding peritoneum of the diaphragm. This may be done very rapidly by the use of a nailbrush with the bristles cut very short. The peritoneum which has been denuded of its endothelium in this way throws out abundant lymph and makes extensive adhesions, which later are filled with new capillaries. The operation seldom accomplishes the object for which it is intended in a satisfactory way, because it is commonly used as a last resource when changes in the liver have become too far advanced. The operation performed before ascites has become a disturbing feature is sometimes distinctly of value, particularly when the omentum is fixed to structures extra to the peritoneum.

> The benefit of the Talma operation for Banti's disease is due to the laparotomy and the resulting hyperemia rather than to the omentopexy. The latter helps, but the hyperemia from the laparotomy is the main factor, as

determined in the course of 10 such cases. In operating the writer aims to induce hyperemia as much as possible and to remove all traces of the ascites. If the kidneys are functioning defectively, absorption of ascitic fluid left behind may prove fatal. He knows of two such deaths, and warns that pronounced kidney disease contraindicates the operation, and that in all cases the general anesthesia should be as slight as possible. Bogojawlensky (Zentralbl. f. Chir., Feb. 27, 1909).

Three cases in which the writer followed Ruotle's method of treating chronic ascites with cirrhosis of the liver by suturing the peripheral end of the saphenous vein, severed 8 cm. above its mouth, to the peritoneum just above Poupart's ligament. In the first case, a man of 38, the patient is well, with no return of ascites after the operation a year ago; in this case omentopexy, decapsulation of both kidneys, and continuous abdominal drainage had failed to cure. In the 2 other cases the ascites was the result of pericarditic pseudocirrhosis of the liver; here none of the operations done, including the Ruotle, gave relief. T. Soyesima (Deut. Zeit. f. Chir., April, 1909).

Case in which the saphenous vein was severed and carried up into the peritoneal cavity through a subcutaneous tunnel. The condition was immeasurably improved, although at first there was much edema in legs and lower trunk. Toussaint (Gacete de la Acad. de Med., Mexico, Jan.-June, 1917).

See also the article on ASCITES in the second volume.

Surgery of the Mesentery and Omentum.—Aside from surgical affections which involve the mesentery along with the intestines, the former suffers from surgical affections peculiar to itself, more especially solid tumors and cysts in the omentum and mesenteric folds. They do not, as a rule, cause acute or complete

ileus, but cause pressure symptoms, and if left alone tend to set up low-grade peritonitis and adhesions to neighboring viscera.

These growths should be extirpated whenever operable. Cysts with dense adhesions and chylous cysts can only be managed by drainage.

SURGICAL DISEASES OF THE INTESTINES.—Ileus.—Most of the conditions which require surgical intervention for the intestine, excepting traumatisms, are brought about by ileus or intestinal obstruction of some form. This is not the place to discuss the manifold agencies which produce obstruction, nor their recognition before operation. Once acute obstruction is evident, the surgeon is usually obliged to open the abdomen, his course afterward depending on the nature of the obstruction. In conditions like intussusception, volvulus, intestinal hernia, or obstruction adhesions, the obstructed loop is released, and steps described for the separate conditions are taken to prevent a recurrence of the trouble. If the mesentery is too long, or the intestine too mobile, a reef may be taken in the former, or the latter may be anchored to the abdominal wall or excised. If the intestine has become strangulated and is gangrenous, enterectomy is indicated with secondary anastomosis. If the obstruction is from foreign bodies, as with round-worms or gall-stones, for instance, the substance should be worked back to an empty portion of intestine, and an enterectomy or colectomy for foreign bodies performed. If the loop of intestine shows serious changes as a result of obstruction, a temporary artificial anus may be advisable. Excision is seldom required in such cases. In

cases of acute ileus from any cause secondary peritonitis may develop and require treatment (see Peritonitis). While acute ileus may result from stricture or tumors, such conditions are much more apt to produce chronic stenosis, which ultimately if left alone will produce chronic ileus. Such cases naturally tend to come to operation before ileus develops. Benign growths and cysts of the mesentery, and similar formations which do not compromise the integrity of the intestine may be removed without much interference with the latter. Tumors of the gut itself necessitate excision of the latter with secondary anastomosis, or establishment of artificial anus. Tuberculous strictures are treated by enteroclusion, or enterostomy for drainage, excision being, as a rule, contraindicated. The same is the alternative in inoperable carcinoma.

Surgical relief of obstruction is the only final salvation for life, and should be instituted early before the patient has absorbed a lethal dose of poison. The only excuse for the responsible physician is the refusal of patient to accept his advice. An inviolable law should be to keep everything out of the stomach. Gastric lavage should be practised to delay serious symptoms until operation can be done, and the lost body fluids replaced by proctoclysis and hypodermoclysis both before and after operation. Murphy's method with resection of any area of damaged intestinal wall is ideal in early cases in the hands of a good technician, but it takes time and adds shock in late cases. The newer method of McKenna, of direct surgical drainage of the high intestinal area by a quick enterostomy high up in the jejunum, tides the patient over the crisis of acute toxemia. Six or eight weeks later, with the patient in good con-

dition the damaged and obstructed area can be resected. J. N. Jackson (Mo. State Med. Assoc. Jour., Sept., 1917).

After abdominal operations there is usually stasis for 24 hours, which acts as a protective measure. Enemas are given the day after operation. If there is no relief, **lavage, laxatives,** hypodermic injections of **pituitrin** or **eserine** are given during the second night and third day. If these do not bring relief, it is concluded that the obstruction is complete. The patient vomits and is toxic. On the evening of the third day or the morning of the fourth he is taken to the operating room and the incision opened. If there is general peritonitis an enterostomy is made without exploration. If there is no peritonitis, exploration is made and the cause, which is usually an adhesion, is removed; then, of course, enterostomy is not necessary. If operation is delayed until late in the fourth day, toxic paresis may complicate the existing conditions. C. H. Mayo (Annals of Surg., lxvi, 568, 1917).

In performing enterostomy for postoperative obstruction, without an anesthetic, a few stitches are removed, the peritoneum opened, and the first distended coil of intestine which presents seized. Into it a purse-string suture of chromic catgut, in a circle at least ½ inch in diameter, is placed rather deeply. With the intestine held up by grasping the suture at 3 different points, a hole is burnt through the center of the circle with the Paquelin cautery, using the pointed tip. A rubber tube is then immediately passed through. The gut being elastic a tube twice the size of the opening may be used. The purse-string is now tied, inverting the margin. If conditions permit, a second purse-string is also introduced. It is a good plan, when possible, to either stitch omentum about the tube or puncture the omentum and pass the tube through it. The tube is secured from slipping with strips of adhesive plaster. J. W.

Long (Jour. Amer. Med. Assoc., Mar. 17, 1917).

In intestinal obstruction following pelvic operations, 3 stages can be noted, those of onset, obstruction, and toxemia. Pain, distress, and vomiting, not relieved by gastric lavage or by enemata, are diagnostic signs, and if present, operation should be performed immediately. But often there is a delay of 24 hours before operation is done. Anspach (N. Y. Med. Jour., June 22, 1918).

Analysis of 245 consecutive cases of intestinal obstruction. Of the 217 patients operated on, 76 died, a mortality of 36 per cent. The operations varied from such simple procedures as the untwisting of a volvulus or division of a constricting band to resection of several feet of gangrenous bowel. The results seemed to depend far more on the condition of the patient at the time of the operation, the long time elapsed since onset of symptoms of obstruction, and the condition of the bowel, than on the nature of the surgical operation. Finney (Surg., Gynec. and Obstet., May, 1921).

Volvulus.—Volvulus most often occurs in the pelvic colon, and consequently does not belong to this group of articles, but it may occur in the sigmoid or cecal region. In the latter case, after untwisting the volvulus and separating any peritoneal adhesions, a rectal tube should be passed and the poisonous contents of the volvulus massaged gently but rapidly toward the rectum, provided that no gangrene of the volvulus be present. The prevention of recurrence by approximation to the anterior abdominal wall by Roser's method is uncertain, and the author favors complete excision of the part of the bowel engaged in volvulus, as this can readily enough be spared, and an end-to-end or lateral anastomosis of the remaining segment of bowel ful-

fills the indication. Volvulus of the cecal region occurs when there is a congenital form of defect giving a sort of mesocecum which may be quite long. Excision of the cecum and intestinal anastomosis are preferable to any attempt at preventing the recurrence of twisting of the cecum.

Volvulus of the small intestine occurs most frequently when the coil of bowel is caught by an adhesion band, and peristaltic progress may loop the bowel in such a way as to cause torsion.

> In sigmoid volvulus the writer sutures together, side to side, the lowest parts of the loop just untwisted. The opening must be 6 or 8 cm. long. The loop above is thus functionally excluded, and finally almost shrivels away. C. Pochhammer (Zentralbl. f. Chir., Feb. 14, 1920).

> The **Grekow-Kummell invagination method** for the radical cure of volvulus of the sigmoid flexure has certain definite advantages over resection. It is simple and brief and permits of both total removal of the flexure and absolute asepsis. The mobilized portion invaginated in the rectum sloughs off spontaneously and is expelled in a few days. Lange (Zentralbl. f. Chir., Oct. 30, 1920).

Localized paralysis of the bowel occurring in typhoid fever may lead to this twisting of the bowel upon itself, and the twisted part can best be excised if the patient's condition allows it.

Intussusception.—In a child with the patient under an anesthetic, an intussusception can sometimes be reduced by the hands on the abdomen, but the last inch is very difficult of reduction, and we are likely to do damage by persistent efforts. There is the same objection to water injection, as we cannot know whether the last inch has been reduced or not.

Furthermore it is very easy to rupture the bowel of a child. We may reduce an intussusception better through a very short incision, even though children bear the operation so badly. Perhaps it is best not to apply many of the resources for intussusception described in the older textbooks, with the exception of operation by immediate laparotomy. There is no occasion in this article to describe the many varieties of intussusception, because the principles of treatment are practically the same in all. Reduction of intussusception is so likely to be followed by recurrence that operation is an addition that is preferable in many cases. The part of the bowel engaged in intussusception is of no value, and consequently excision of the bowel with anastomosis is in order, unless the patient is in a desperate condition, in which case we may simply approximate any two loops of bowel above or below the intussusception and unite these in the common way with a Lembert suture.

Intussusception cannot progress beyond the point at which such anastomosis has been made.

In emergency cases of intussusception, with the patient *in extremis*, the author likes the method of making a quick lateral anastomosis immediately above and below the area involved in the intussusception. If two traction sutures are used for approximating the loops of bowel to be anastomosed the work can be done very quickly and with little traumatism.

The results of this procedure in emergency cases would seem almost to justify the simple resource as a regular procedure. Intussusception cannot progress beyond the sutured area. The

invaginated part of the bowel in the intussusception may slough or undergo subsequent atrophic changes without adding a serious feature.

> The diagnosis should be followed by immediate operation which should be performed with the minimum amount of handling of the intestine and traumatism. The best incision is one that splits the rectus at the junction of its middle and inner third, and extends one-third above and two-thirds below the umbilicus. If possible the tumor mass should be grasped with two fingers and brought out through the incision. Reduction is successful in between 80 and 90 per cent. of cases. Any other procedure is so unsatisfactory that every effort should be made to complete reduction. If it fails, resection with end-to-end anastomosis probably offers the best chance of recovery; but the mortality is high, as the case is usually a neglected one. Formation of an artificial anus is attended with practically 100 per cent. mortality. Attempts to prevent recurrence by anchoring or shortening the mesentery are doubtful and prolong the operation. In closing the abdomen, tension sutures of silkworm gut should be inserted through the skin and aponeurosis, in addition to the layer sutures. Special efforts should be directed to combat shock. B. T. Tilton (N. Y. Med. Jour., Oct. 7, 1916).

Typhlitis.—Not readily distinguishable from appendicitis, and is usually treated by simple opening of the abscess and drainage.

Meckel's Diverticulum.—One of the remains of the vitelline duct is sometimes attached to the convex border of the intestine, and varies considerably in range, as well as in character. In some cases it closely resembles the part of bowel from which it springs. Consequently all varieties call for their respective forms of treatment.

Sometimes the entire tube remains as an opening at the umbilicus, but more commonly we have only the patent part of the tube near the bowel with a cord-like remainder extending to the umbilicus. Foreign bodies may escape into this diverticulum, or ordinary intestinal contents may result in exciting inflammation. Adhesions may produce angulation of the tube, interfering with circulation and leading to infection. Sometimes the diverticulum acts as a constricting band in intestinal obstruction, in which case it takes part in acute inflammatory process and may become gangrenous. Volvulus of the diverticulum may occur.

Colonic Diverticula.—These may occur at any point, and often consist of anatomic defects opening into epiploic appendages. Increased pressure within the bowel at any time may lead to considerable enlargement of one or more such diverticula, and later with obstruction and inflammation.

As in the case of one of the writers, diverticulitis, particularly when situated about the sigmoid region, may result in perforation into adjoining structures. In the writer's case there was penetration of the wall of the bladder and also of the adjoining segment of the ileum. Resection of the whole area of the diverticula including practically the whole sigmoid, and also of the tissues of the bladder and ileum by W. Wayne Babcock resulted in perfect recovery. EDITORS.

Epiploic appendages when twisted upon their long axes may become congested and even gangrenous in very fleshy patients, but the treatment is simply for abscess which follows.

Diverticulitis of the sigmoid region is the most common, giving symptoms quite similar to those of appendicitis, excepting for location of tender-

ness. The infiltrated tissues may respond to external applications of heat or cold, but frequently we must operate for the abscess which remains.

> Report of several cases of diverticulitis. The writer has had success with temporary colotomy to rest the bowel, with subsequent resolution of the inflammatory process, so that the colotomy wound could be closed and the lower part of the gut was able to function again. He has also inverted the projections, converting them into polypi. Important to keep the bowels regular and to have the patient stop eating when symptoms develop, if medical treatment is used. Turner (Lancet, Jan. 17, 1920).

Wounds, Perforation from Within, etc.—In cases of solution of continuity in the intestine, whether from penetrating wounds from without or perforation from ulcers within, the course of procedure is the same. Laparotomy is performed and the wound or perforation sutured, unless the wounds are multiple and so close together that suture would cause too great a reduction of caliber, in which case anastomosis may be necessary.

TYPICAL OPERATIONS OF THE INTESTINE.—Enterorrhaphy. —This term is applied to suture of the intestine for wounds or ulcers which are not extensive enough to require excision and anastomosis. The chief amount of intervention is in connection with the external incisions and examination of the intestine to determine the extent of the injury, which may involve more than the bowel itself. Hemostasis and cleansing of the peritoneal cavity will necessarily be required in traumatism from without, as well as in perforating ulcer from within. It will often be necessary to incise the mesentery in order to complete the examination,

and these incisions must always be sutured in such a way as to leave no point uncovered by peritoneum.

Perforation may, as a rule, be sutured without preliminary excision of tissue. The suture should run parallel with the long diameter save when the traumatism is near the pylorus. In this locality it should be applied in the transverse diameter. It is exceptional for an external traumatism to consist only of a single perforation of the intestine, for, as a rule, not only is the bowel itself penetrated doubly, but other portions of intestine and mesentery are involved in the knife or bullet wound. Hence single isolated trauma occurs most naturally from the internal perforations.

Multiple perforations of the bowel and mesentery are adaptable for suture, no matter how numerous, if they are not too close together; but, when a portion of bowel is, so to speak, riddled by bullet or other wounds, it should be excised, unless the author's resource in one case quoted above introduces a principle in addition.

For suturing perforations a few points of interrupted Lembert silk or linen suture are usually sufficient. In multiple perforation or when there is suspicion of such, it is advisable to suture as soon as the wound is located, and before proceeding with further examination.

The rule for determining the possible limit of suture in contrast to excision is this: if the suture of one or more openings does not diminish the caliber of the intestine by more than a third, suture is indicated in place of excision.

In perforation from typhoid ulcer

multiple traumatism is unusual, and the lesion in most cases is seated not far from the ileocecal valve. Owing to the general state of the patient the operation must be rapidly done, as a rule. An appendicitis incision usually suffices.

The perforation is closed at once by a few interrupted sutures, or a purse-string suture. Cases of typhoid perforation do occur in which, either from the size, number or complications of the lesion, enterostomy or enterectomy is required, but the condition of the patient sometimes makes it desirable to quickly fasten the bowel opening near to the external opening, and to do a secondary excision operation after recovery from the typhoid. The friable character of tissues distended with serous infiltrates also makes this expediency work necessary when the friable tissues refuse to bend freely to sutures. Even after simple suture it may not be advisable to close the abdominal wound, in contradistinction to the course pursued in suture of external wounds. The presence of peritonitis with adhesions may make it advantageous to leave the lower angle of the wound open for the purpose of a little drainage.

Review of the literature of intestinal perforation in typhoid fever showed that those operated upon in which perforation was found consisted of 269 cases (from 1903 to 1909); 156 of this number resulted fatally, giving a mortality of 57.99 per cent., while Harte and Ashhurst (all cases from 1884 to 1903), in a similar study, found 311 cases, with a mortality of 73.31 per cent. Charles Bagley, Jr. (Surg., Gynec. and Obstet., Aug., 1911).

In a search through the literature since 1903, the writer found 133 reported cases of typhoid fever in which perforation occurred and was closed by suture. Of this number 68.5 per cent. died and 31.5 per cent. recovered. G. D. Head (Jour. Minn. State Med. Assoc., Aug. 1, 1911).

Enterectomy.—Excision of portions of intestine is performed for a great variety of conditions, such as traumatism, malignant tumors, actual or impending gangrene, etc. It is indicated, therefore, as an operation of choice or necessity in many of the conditions which constitute or give rise to ileus. The part to be removed may vary in length from two or three inches to a number of feet. In enterectomy, as in similar operations, the actual operation requires much less time and a much simpler technique than the secondary stage of restoring the continuity of the intestine. There is in fact but one technique for the former, while the latter is not only practicable by quite different operations, but each operation may be performed by a number of different methods.

For the performance of the enterectomy proper, it is necessary to excise a portion of intestine with a certain amount of mesentery. After the external incisions and exploration of the abdomen the portion of intestine to be excised is, if necessary, freed from adhesions. This coil of intestine should be milked into the portions of the gut continuous, for which purpose the fingers of assistants must be used. After one-half of the coil is thus emptied in one direction the fingers should compress the gut to prevent re-entrance of intestinal contents; the other extremity is then similarly treated. Instead of the fingers of assistants, clamps may be applied, one at either end and

some inches beyond the segment of gut to be excised. Loops of gauze may also be used, but in such a case the mesentery must be penetrated, and it is best to use the fingers of assistants as far as possible.

Before excising, the mesentery must be ligated off close to the intestine,—about one inch distance. An approximate rule is to place a catgut ligature for every inch of mesentery. Another is to ligate less rather than more mesentery than is apparently called for. This is done on the principle of overcorrection, because if too much mesentery is sacrificed the edges of the anastomosis to be performed may suffer gangrene from interference with blood-supply.

When all preliminaries have been completed the gut with its mesenteric stump is removed by means of the scissors.

> Case of resection of 300 cm. (10 feet) of the small intestine and the cecum, with 20 cm. of ascending colon, owing to extensive ileocecal tuberculosis. The patient left the hospital at the end of the fourth week, having about 3 stools a day, but 2 months after operation he returned with a severe cold and died shortly afterward of acute tuberculosis. Post-mortem examination showed the abdomen in excellent condition. The remaining small intestine up to the duodenojejunal juncture was only 5 feet, 7 inches, in length. Canaday (Annals of Surg., lxix, 425, 1919).

> Report of experiments supporting Payr's disinfecting method of mucous membrane of the intestine by painting with a 5 per cent. solution of iodine. In 67 per cent. of cases the iodine produced sterility, and in 33 per cent. the number of bacteria was decreased. The procedure is especially of value in the lower parts of the colon. L. Frankenthal (Beitr. z. klin. Chir., cxx, 614, 1920).

> Report of 282 consecutive cases of acute intestinal obstruction operated on, comprising 170 cases of obstruction due to external hernia, 42 cases of carcinoma, and 70 other cases of obstruction. **Saline infusion** and **morphine** were used.
> The mortality was 9.3 per cent. in the cases not requiring resection and 47.8 per cent. in those requiring resection. Experience in determining whether the intestine is viable or not is important. When the walls are of an abnormal color and, in addition, feel limp and offer no sensation of firmness to the fingers, recovery is unlikely. E. R. Flint (Brit. Med. Jour., May 21, 1921).

Enteroanastomoses. — These methods of restoring continuity of the intestine after enterectomy comprise three distinct types. The first and most natural is end-to-end anastomosis or suture, which in most cases is the operation to choose.

The second type is known as the side-to-side laterolateral or simply lateral. It differs in scope from the preceding chiefly because it may be used between the small and large intestines, and small intestines and stomach.

> In acute intestinal obstructions from adhesions, unless the adhesions can be easily broken up, it is better to leave them alone. The loops above and below the obstruction should be joined by side-to-side anastomosis. The writer describes 7 cases in which he did this, with recovery and good results in 6 instances. If it is considered best to resect the excluded segment, this can be done later after the general condition has improved. The intestine may be twisted when bound down by bands, and the circulation be so impaired that the slightest traction causes rupture. Ingebrigtsen (Norsk Mag. f. Laegevid., Feb., 1921).

The third type is known as end-to-side or terminolateral, or simply as

the implantation method. It is restricted in practice to implantation of a cut end of small intestine into the stomach or colon. The first-named has already been considered in part under pylorectomy. The latter is specifically known as ileocolostomy, or ileosigmoidostomy.

Gastroenterostomy.—This operation consists of a lateral anastomosis between the stomach and some portion of the small intestine, either the duodenum or jejunum. According as the intestine is united to the anterior or posterior stomach wall the operation is known as anterior or posterior gastroenterostomy.

The operation is indicated in certain cases of gastric or duodenal ulcer, either as a primary resource or one secondary to pylorectomy or gastrorrhaphy. Generally speaking the operation is one of necessity when milder measures have failed or are likely to fail. Minor indications for gastroenterostomy are found in contraction of the pylorus from swallowing corrosive poison, in some cases of congenital stenosis of the pylorus, and finally in certain cases of cancer in this locality, as a palliative when pylorectomy cannot be performed.

The operation is contraindicated in so-called medical diseases of the stomach, however severe these may be.

The ideal operation is one in which the opening is made as nearly as we can to the pylorus and the proximal loop of jejunum, thus utilizing the part of the stomach which is commonly the lowest during the process of digestion. This will allow free regurgitation to the alkaline intestinal juices. Anastomosis with the cardiac part of the stomach would allow acid contents to escape in case of good digestion, and defect of pyloric digestion would be the result. In addition, cases have been reported in which jejunal ulcer has followed the forming of an opening at a point where acid contents could injure the tissues. The choice of procedure in gastroenterostomy at the present time is certainly the so-called posterior no-loop operation, but the author has referred to older operations which are necessary at times. Even with ulcer of the stomach in the cardiac end of the stomach, the posterior no-loop operation should be made with the pylorus, if possible, to avoid the effects of gastric acidity at some distant point from the pylorus. The posterior no-loop operation is performed by making an opening through the transverse mesocolon in the usual way, avoiding the middle colic vessels. The posterior surface of the stomach being exposed, a portion near the pylorus part is chosen and drawn through the opening. The jejunal flexure close to the duodenum is found beneath the left of the mesocolon, and the proximal loop is employed for completing the gastroenterostomy, in such a way that when the parts are released from the fingers or clamps the intestine will hang in a direction which is almost vertical, but with a slight inclination toward the left or right, in a normal line of the long axis of the individual jejunum. This is the essential part of the posterior no-loop operation.

Of 273 cases in which the writer had resorted to gastroenterostomy, 170 were male and 103 female. The average age at which the operation was done was 44.3 years for males and 41.5 years for females. In those

cases seen shortly after operation in which one would not expect total restoration of gastric function, 20.9 per cent. were free from complaint; 49.8 per cent. were clinically comfortable, and in 87.89 per cent. subjective benefit had resulted. F. Smithies (Surg., Gynec. and Obstet., xxvi, 275, 1918).

The writer strongly advises location of the anastomotic orifice at the dependent point of the pyloric vestibule, as near as possible to the greater curvature of the stomach. Posterior gastroenterostomy as ordinarily performed does not always permit of recognition by the operator of the exact point of the stomach which he is bringing up through the narrow slit in the mesocolon. To obviate this, he recommends Lardennois and Okinczyc's procedure of stripping the omentum from the colon, which allows the operator to expose the entire posterior surface of the stomach. The anastomosis having been effected, the margins of the opening in the mesocolon are simply sutured through the posterior cavity, and the great omentum is brought down over the transverse colon. P. Duval (Presse méd., Mar. 13, 1919).

Regulation of the size of the gastroenterostomy opening recommended. Where there is gastric atony, the contents will pour out too quickly unless the opening is small; yet it should be at the lowest point. With hypertonicity and a need for resting the stomach, the opening should be large and in the antrum, near the lesser curvature. If later required, the pylorus can then be closed. Métivet (Presse méd., Jan. 28, 1920).

The cause of jejunal ulcer after gastroenterostomy is the pouring of acid gastric juice directly into the jejunum, which is physiologically fitted for only alkaline contents. Accepted treatment of jejunal ulcer after gastroenterostomy is to disconnect the gastroenterostomy and perform a pyloroplasty. If a pyloroplasty had been done in the first instance, the jejunal ulcer would have been avoided.

The writer had a case of jejunal ulcer that occurred on the mesenteric border of the jejunum opposite the gastroenterostomy. J. Shelton Horsley (Trans. So. Surg. Soc.; Jour. Amer. Med. Assoc., Jan. 15, 1921).

Stress laid on the superiority of trans- and supra-mesocolic gastroenterostomy over ordinary posterior gastroenterostomy. When the former is performed in simple cases it is not necessary to bring the transverse colon to the surface of the body. In difficult cases this allows the surgeon to operate outside the abdomen, and to place the opening in a good position. If the operative indication is clear, if exploration of all the posterior surface of the stomach is not necessary, and if the gastroenterostomy is only the first stage of a gastrectomy, the gastrocolic ligament is depressed with the finger and the posterior wall of the stomach is exposed. If a very wide exploration of all the posterior wall of the stomach is necessary the intercolo-omental exposure of Duval is done. If pyloric exclusion by section is indicated and there is no suitable area on the posterior wall of the stomach to make the anastomosis the greater curvature is stripped of its vessels. R. Toupet (Presse méd., xxix, 253, 1921).

When postoperative jejunal ulcer occurs, the basis for it is usually laid during the first few weeks or months following gastroenterostomy, owing to neglect of dietetic precautions. Light and more frequent meals than normally are indicated. In other respects the diet should be regulated as in cases of gastric hypersecretion. The marked acid-combining capacity of casein and the inhibitory effect of fats on gastric secretion are emphasized. Cottage cheese, thoroughly mixed with milk or cream or softened and loosened up by stirring in beaten whites of eggs, with sugar, should be used plentifully, beginning a few days after the operation. Of the fats, that of boiled beef, fresh and melted butter or, still better, vegetable oils (from 1 to 2 table-

spoonfuls after eating), are indicated. The antacid effect of the oils is more marked if taken separately than if mixed with the food. For the first 3 weeks after the operation, the writer recommends a diet of boiled milk, fresh cottage cheese, 2 or 3 soft boiled eggs, fine wheat bread, butter, gruels and plain rice dishes. Later, mild cheese, mashed potatoes, vegetables passed through a sieve, and cooked fruits may be added. This diet should be adhered to for from 6 to 8 weeks, all meat or raw vegetables being excluded. Favorite dishes and appetizing odors should be scrupulously avoided, to obviate "psychic" gastric secretion. Von Noorden (Therap. Halb-Monatsh., Apr. 1, 1921).

If the edges of the cut mesocolon are fastened to the stomach wall before completing this gastroenterostomy, it will obliterate the opening in the mesocolon, and this is desirable for avoiding subsequent hernia, if the patient's condition allows us to follow ideal technique. When adhesions or extensive scarring or other mechanical reasons make the posterior no-loop operation of gastrojejunostomy difficult, we may use gastroduodenostomy, instead. The anterior wall of the pylorus is joined with the descending part of the duodenum, but where we suture the mesocolon to the stomach it avoids the danger of subsequent hernia.

It is practicable to insert a previously swallowed Rehfuss gastroduodenal tube well into the jejunum and to commence at once, on the operating table, the feeding of peptonized milk, dextrose and alcohol mixtures. Immediate jejunal feeding after gastroenterostomy is not only to be recommended in the operations performed for stenosis, but should be tried in all types of cases. Andresen (Annals of Surg., May, 1918).

Anterior Gastroenterostomy. —This, the original procedure, has been replaced in most cases by the posterior operation, but is still performed when the posterior wall is unaccessible by reason of adhesions or organic disease. A fairly good rule is for the surgeon to do whichever operation he can do most easily in any given case, but the anterior operation gives more postoperative complications. The operation is as follows :—

After the stomach has been fully exposed, its anterior wall is so grasped that the fold which is to be the seat of the anastomosis runs obliquely across from right to left, and from below upward. The intestine is similarly grasped about eighteen inches below the duodenojejunal junction and the two structures placed side by side.

The anastomosis is then carried out as in all similar procedures, onehalf the outer plane of sutures being inserted before the incision is made. Details of technique will be considered under the posterior operation.

Posterior Gastroenterostomy.—The external incision is that used for other operations on the lower portion of the stomach and the pylorus, passing through the right rectus by blunt dissection, the posterior sheath and peritoneum being divided together. The incision is largely an exploratory one, for despite the evidence of a pyloric ulcer, for example, the entire stomach and duodenum with the neighboring viscera must be examined for complications and possible contraindications. The jejunum must also be examined with especial reference to its relations with other organs. The natural direction should be learned, for this may be to the right, left, or directly downward, and

in bringing the intestine in contact with the posterior wall the original direction must be conserved.

In order to gain access to the posterior wall it is necessary to go through the transverse mesocolon, the incision being ample enough to enable the posterior wall to be drawn outward; but the incision in the mesocolon, to avoid opening large blood-vessels, should be first made small and then enlarged by stretching with the fingers.

Generally speaking the portion of this wall to be selected for anastomosis is at the lowest point of the organ, which is considerably nearer to the pylorus than to the cardia and fundus. The author likes to cut through the ligament of Treitz when approaching the posterior stomach wall. This brings one to a convenient part of the jejunum for the no-loop operation. He prefers traction sutures rather than instruments for approximating stomach and ileum during operative procedure. The portion to be incised for the anastomosis is pinched up in a direction corresponding to the natural direction of the jejunum itself. The latter is also grasped an inch or two below the duodenojejunal junction. As in all such anastomoses, a portion of the outer plane of sutures is introduced before the incisions are made. This is a continuous seromuscular suture, intended to fix the two structures together and furnish a guide to the incisions. The latter, some three inches in length, are not simple linear incisions, but a small spindle-shaped portion of tissue is excised. The two openings thus made are now sutured together by through-and-through stitches of the penetrating type, the two posterior

margins being first united, and then the anterior margins, the inner layer of sutures being thus completed. The fingers or clamps are removed, and the outer plane of serous sutures completed.

In performing the posterior operation the writer advises that the operator locate the peritoneal suspensory ligament or band which extends from the transverse mesocolon to the upper part of the jejunum. Immediately above this band, in the mesocolon, is an area in which there are no important blood-vessels. The suspensory band having been stripped away, and a transverse incision made in the above-mentioned area of the mesocolon, the posterior aspect of the stomach may be drawn through this opening and the denuded jejunum attached to it, the attachment thus being without strain or loop and following the normal direction of the jejunum. Mayo (Annals of Surg., Jan., 1908).

New method of gastroenterostomy accompanied by less traumatism to tissues than where clamps are used, sure to be free from postoperative hemorrhage, and more readily performed. A celluloid suture is inserted through the stomach and intestine at each end of the sites chosen for the new communication. By keeping traction on these, the jejunum and stomach are kept in close approximation. The usual posterior stitch is next introduced. The peritoneal cavity is then walled off and incisions made in both viscera close to the line of suture exposing the blood-vessels. These, usually 5 or 6 in number, are doubly secured with hemostats and the mucosa opened between them. Taking first the posterior wall, each pair of vessels, one gastric and one intestinal, is ligated with a single strand of chromic catgut, after drawing the edges together by means of the two forceps in closest proximity. These ligatures not only prevent any hemorrhage, but hold the edges of

the mucosa in firm apposition. The anterior edges are drawn together by beginning at the end farthest from the surgeon. The 2 forceps which lie opposite each other are held together by an assistant. The right end of the ligature is passed around the forceps on the intestine from right to left, the left end is passed around the forceps on the intestine from left to right so that the ends emerge between the forceps, beneath the loop of the ligature. The forceps are now brought parallel to the long axis of the wound, and rolled toward each other, inverting the mucous edges of the wound. Each succeeding pair of vessels is dealt with in the same way. The rest of the procedure is much as in the usual operation. Of the last 40 patients, 38 recovered and 2 died, these 2 having inoperable carcinoma and succumbing to exhaustion and pneumonia. F. T. Stewart (Annals of Surg., lxvi, 334, 1917).

Roux's Operation.—The Y-operation of Roux differs notably from the typical procedures just enumerated, being a combination of the anastomoses, both being examples of implantation of terminolateral anastomoses. The jejunum having been divided across, the peripheral segment is implanted into the posterior surface of the stomach, while the proximal segment is implanted into the jejunum.

It is no longer held desirable to use mechanical devices in most gastroenterostomies, although such aids were of great importance at one time in giving us confidence to advance to a simpler technique.

Gastroenterostomy is liable to be succeeded by certain typical complications. Among these are hemorrhages, sometimes inexplicable, but now generally believed to be due frequently to overlooked ulcers, or to imperfect suturing, or to the use of too-fine suture material which cuts out when the patient vomits. In bleeding ulcer of the stomach it is sometimes extremely difficult to recognize all of the bleeding surface while the tissues are held in tension. Relaxation of tissues and pressure on the viscera with the fingers or with gauze may start a free bleeding which localizes the ulcerated area. Postoperative ileus may develop, which may be due to obstruction from adhesions, to internal strangulation, or to angulation of bowel, particularly in the anterior operation, if the loop is not supported by side sutures in the omentum.

Aside from vomiting, which is symptomatic of this obstruction, we may have a non-obstructive type which supervenes at a late period (one or two months following operation). The nature of the vomiting is not always clear, but, since operators have sought to preserve the natural direction of the jejunum, cases of obstruction and vomiting have been much less frequent.

A complication of considerable gravity is peptic ulcer of the jejunum, attributed once to the action of digestive enzymes, but now regarded as having a common origin with ordinary gastric and duodenal ulcer, viz., hyperacidity (hyperchlorhydria) and toxic injury of terminal arteries. To lessen the frequency of this complication it is advisable that every patient to be operated upon be first treated for hyperchlorhydria. Peptic ulcers of the jejunum run a similar course to that of ulcers higher up, terminating at times in perforation.

Condition of the patient one year or more after gastroenterostomy in 175 cases, 150 benign, 25 malignant:—

Benign Cases (150).—The immediate mortality (death within thirty-five days) was 10 per cent. Eighteen died within the first year (12 per cent.); 22 died of their gastric disorder within five years (14.6 per cent.). Six patients are alive, but have been operated upon within one year.

Of the 126 patients who survived the operation, and have been under observation for one year or more, 81 (or nearly two-thirds) were reported as entirely recovered, or well; 8 as much better, and 31 (nearly 1 in 4) as little or no better. Of the 150 patients 89, or 60 per cent., were much better or entirely well; fully 30 per cent. died or were little or no better at the time of report.

Twenty-five *cancer cases* are reported, 20 being in men. Ten patients died within one month of the operation, an immediate mortality of 40 per cent. One is still living, two years after operation, another six months, and another four months. Ten patients lived more than four months after operation. Six of these were temporarily much improved, and gains of weight ranging from eighteen to forty-seven pounds are recorded. Two patients received no benefit at all from the operation. Bettmann and White (Med. Record, Oct. 9, 1909).

In gastroenterostomy the new formed anastomosis is the site of a healing ulcerated surface for a period of 14 days, and for the first 5 or 7 days, the process is largely destructive. For the first 2 weeks, the diet should be as light as is compatible with maintenance of strength. Flint (Annals of Surg., Feb., 1917).

The new train of symptoms sometimes following gastroenterostomy is usually due to peptic ulcers in the stomach or bowel in the vicinity of the new stoma, or adhesions.

All of these various complications or disturbances usually yield to a liquid diet, large doses of bismuth, and gastric lavage, but when these fail, duodenal or jejunal alimentation is of great benefit. Of 10 such cases 8 were so much improved that no further treatment was necessary. Max Einhorn (Med. Rec., June 16, 1917).

Case of spasmodic occlusion of the anastomotic mouth after gastroenterostomy in which complete success was obtained by administering belladonna. The author is satisfied that his patient like Zweig's was vagotonic, with gastric hypertonia. L. Urrutia (Arch. des mal de l'Appar. digestif, lx, 84, 1917).

Fatal postoperative diarrhea sometimes occurs. Its nature is obscure and seems to depend upon derangement of bowel function due to shock to the sympathetic ganglia.

End-to-end Anastomosis after Enterectomy.—This may be effected by suture, or Murphy's button. The suture methods in use comprise the simple direct suture, the combination of suture and invagination, the Connell method, etc.

Simple Suture.—The mesentery is first united by transfixing both the cut edge of the gut just beside the mesentery, and then the latter close to its insertion. The same through-and-through suture is then passed in the reverse order through the opposite mesentery and gut. A duplicate suture is now passed through the other side, or the same suture may have its other end threaded in a needle and be used for this purpose. When this suture is tightened the gap in the mesentery is closed with approximation of the cut ends. The remaining step is suture of the latter, and this may be done by carrying the original two-tailed mesenteric suture from its knot around the circumference of the gut on either side until most of the circumference has been sutured. The opening which remains is closed with an outside Lembert suture. The rent in the mesentery is closed with a few points of catgut.

Intestinal anastomosis by invagination, cuff and suture, is probably the simplest, quickest, safest, easiest method and the freest from unpleasant complications.

The proximal end should extend from 1 to 1½ inches into the distal end in end-to-end anastomosis, though less in lateral anastomosis.

The invaginated ends and portions of gut eventually atrophy without stenosis.

Fine round needles, silk or linen thread, and interrupted rather than continuous sutures should be used. B. M. Ricketts (Trans. West. Surg. and Gynec. Assoc., 1919).

Maunsell's Method.—The divided surfaces of intestine are placed in rough apposition by four traction sutures at equidistant points, the first at the mesenteric insertion. The next step is to introduce a pair of forceps through the intestinal wall from without inward, and to this end a slit is made in the long diameter of the bowel, one (either side) segment opposite the mesenteric insertion and about one and one-half inches from the cut edge. With this forceps the loose ends of the traction sutures, previously twisted together, are tightened with production of an invagination of the distal into the proximate segment, the two serous coats being in contact. In this position the two edges are united with a chromicized-gut suture applied through-and-through, the traction sutures are removed, and the invaginated segment replaced. An external durable Lembert suture is now applied.

Connell Method.—As in the preceding operation, four traction sutures are applied, and the two cut edges of intestine are sutured, one-fourth at a time. The traction sutures which limit each quadrant are tightened in turn, and the intervening intestine joined by applying a right-angled through-and-through suture. As soon as a portion of the gut is reunited one of the tractors becomes unnecessary and is removed. At the close of the suturing the two free ends are threaded within the lumen of the intestine upon a ligature carrier, brought outside and tied, and the knot is then worked back on the inside of the gut.

New method of aseptic enterectomy and enteroanastomosis is described, which is based on crushing with clamps of the visceral layers of the parts operated on. In end to end anastomosis, Kocher forceps are placed at the margins of the previously crushed sections of bowel, and the piece of bowel to be taken out removed by passing the scalpel along the closed forceps. The 2 forceps are then placed side by side, and 2 continuous seroserous sutures carried successfully through the adjoining bowel tissues along one side of the forceps, next round their tips, and finally back again along the other side. The forceps are then removed—the bowel ends having already been united all around except at one point, the point of entrance of the forceps—and a grooved director is passed in and moved from side to side, thus detaching the previously adherent margins of the serous coats, unfolding the mucous and muscular coats, and restoring communication between the two bowel ends. The suture ends hanging out are now tied, thus closing the opening. In laterolateral anastomosis, as in gastroenterostomy, the 2 linear portions of visceral wall to be joined are first crushed; 2 continuous sutures are then passed completely round these portions except at one point, through which scissors are introduced to cut through the serous coats before the sutures are tied. The perfect results ob-

tained were confirmed by post-mortem examinations. Gudin (Paris Méd., Dec. 16, 1916).

Axial or end-to-end anastomosis of the colon has not hitherto been popular because of its high mortality. The author points out that the real reason why axial union often failed is that the arteries supplying the colon pass round in a circular direction with very little anastomosis. Leakage after axial union is generally on the side opposite to the mesentery. All that is necessary to secure a good result in axial anastomosis is to cut the bowel across at an angle of 45 degrees from the mesentery outward, *i.e.*, with more

insertion. The tails are then carried down on either aspect of the intestinal segment to the point opposite the mesenteric insertion, the suture of chromicized gut being applied overhand. The two tails of the suture having been tightened upon the halves of the button, these are then joined and locked. The rent in the mesentery is now repaired and an outside durable Lembert suture applied over the inside suture. Great care is taken to cover the bowel incision with peritoneum at the mesenteric attachment.

Closed.　　　Open.

Oblong Murphy button.
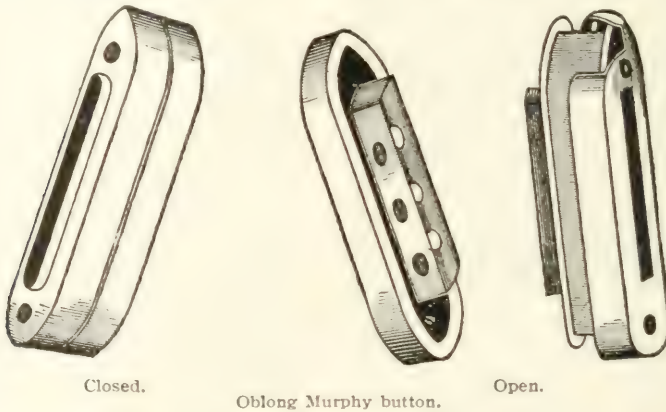
bowel removed on the free than the attached side, thus insuring a good blood-supply to the whole of the sutured edges. The writer has used this method for years, with almost uniformly perfect results. With the resected portion of bowel a wedge of mesentery is removed. The bowels are moved on the second day by a small gruel enema, assisted, if necessary by pituitary extract. P. Lockhart-Mummery (Surg., Gynec. and Obstet., Feb., 1917).

Murphy Button.—Purse-string sutures are applied at either divided segment and tightened upon the halves of the button. The suture for each side is a two-tailed one, and first transfixes the mesentery at its

Lateral Anastomosis.—In this operation there is no restoration of the continuity originally present, but a purely artificial opening is created between the two segments of intestine. Such an operation may be termed an internal enterostomy, which agrees with an external colostomy to this extent: that in each case a fistulous communication is set up. In this connection we need only describe the operations of enteroenteric anastomosis and ileocolostomy, for the gastroenteroanastomoses are considered elsewhere.

This anastomosis may be effected in several ways—preferably by su-

ture, clamps, elastic ligature, or Murphy's button may be desirable in special cases.

Suture.—The loop of intestine is emptied and prevented from refilling by finger pressure, clamps, or gauze loops. Excision having been performed, the two cut ends are closed by the insertion of inverting Lembert sutures, the slack of the mesentery being included in the inversion. A double *cul-de-sac* thus results, the two parts of which are to be joined in the resulting lateral anastomosis. The two ends are apposed for a space of four inches or more, and a single line of Lembert sutures applied at their junction. The segments being now in their permanent position, they are incised close to the suture line with scissors. As a rule, the length of the incisions should be three inches.

A continuous suture of chromicized gut is carried along both sides of the new opening, thus constituting the inside suture plane. The outside plane is completed by a second durable Lembert suture. Of mechanical aids, Murphy's oblong button is the best for general use, the technique being akin to that of the round button for end-to-end anastomosis.

Enteroexclusion.—The temporary operation is not a procedure comparative to enterectomy. It is without some of the dangers of the radical operation, and may be performed rapidly. The operation consists in division of the intestine and lateral enteroanastomosis, or, in the case of the colon, enteroimplantation. A diseased portion of the intestine which would otherwise demand extirpation is then excluded from the intestine. If the distal end is closed the operation is known as partial or unilateral exclusion; but, if it is also made the subject of an anastomosis, the intervention is known as double or complete occlusion. The chief indications are tuberculosis, fistulæ (especially multiple ones), and malignant disease.

Unilateral Exclusion.—No attempt is made to close the excluded loop at its lower extremity, which is just above the anastomosis, as there is no danger of stagnation of feces in this locality. Technically the operation is well adapted for the use of Murphy buttons. No details need be given, as these are identical with the details of anastomoses after excisions. Its chief use is in emergency cases.

Bilateral Exclusion.—Both ends of the excluded loop are closed, and either two anastomoses are made or one end only is anastomosed while the other is left in the external wound. When the operation has been done for actual intestinal fistulæ, both ends of the loop may be closed, as the loop will then be drained sufficiently through the fistulous openings. If exclusion is done for carcinoma it is better to leave one end of the loop in the external wound, for, when the operation has been done for any incurable condition, exclusion must be followed sooner or later by excision.

The writer warns against operations on the intestinal tract in which no outlet is provided for the intestinal mucous secretion. This oversight sometimes leads to fatal results. When stimulated into greater activity by irrigation or infection, the amount of secretion may be enormous, as in colitis, and even result fatally. G. G. Turner (Brit. Med. Jour., iv, 227, 1916).

Where a patient with toxemia only from the small bowel becomes a sur-

gical case, the writer considers the Lane short circuit ileocolostomy the operation of choice, but if, as is usually the case, the obstructed ileum is accompanied by a dilated and atonic cecum, the Mayo right-sided colectomy is the proper operation. The Mayo technique is free from the criticism of the Lane technique, in that the intestines are not handled after the colon has been opened, greatly lessening the possibility of infection, while there is no blind pocket left to become impacted. R. Smith (Surg., Gynec. and Obstet., Nov., 1916).

Actual colectomy must be abandoned as impracticable because of late unpleasant complications. Even after simple ileosigmoidostomy, pronounced anastalsis supervenes, aggravating the toxemia. In what the writer terms physiological colectomy, after the ileosigmoidostomy with side to side anastomosis has been established, the sigmoid is divided in its upper arch as near as practicable to the lower end of the distal sigmoid. The open end of the distal segment is then fixed in the lower angle of the wound and the open end of the proximal colon in the upper angle. Finally, a catheter—afferent— is inserted into the open terminal ileum, the tip being carried into the cecum, and a large tube—efferent—into the open end of the colon. Thus isolated, the colon is irrigated to unload its toxic fecal content and then left to atrophy from disuse. Where a secondary actual extirpation becomes necessary, the difficulties are diminished owing to the atrophy of the colon. The primary mortality from physiological colectomy should be practically *nil*, though as yet the percentage of ultimate recoveries have not been entirely satisfactory. C. A. L. Reed (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 30, 1917).

Enterostomy, Jejunostomy, Ileostomy.—The establishment of an artificial opening in the small intestine is not necessarily for the purpose of establishing an anus *contra naturam*, but may be done simply for relief of distention or, like gastrostomy, for the introduction of nutriment. The only condition justifying this form of intervention is an absolutely irremediable stricture of the pylorus with resulting starvation.

The operation may be done like a gastrostomy, using a tube or catheter. It is preferable, however, to sacrifice the integrity of the intestine by division and anastomosis, leaving a cut end in the external wound. The point selected is in the jejunum, about eight inches below the duodenojejunal angle. The intestine is divided at this point and the central end implanted six or eight inches farther along the gut. The peripheral end is not treated like the stomach cone in gastrostomy, *i.e.,* it is passed out of the external incision, beneath the skin, and out at a special opening (see Gastrostomy). The original wound is closed plane by plane while the fistular wound is sutured to the divided intestine.

Ileostomy is sometimes performed for establishing an artificial anus, necessarily in cases where ileocolostomy or simple colostomy is insufficient for drainage. The lowest possible part of the ileum is selected, the incision being made one and one-half inches above Poupart's ligament. In this operation it is not necessary to divide the intestine, and the technique does not differ from that of ordinary colostomy.

Jejunostomy advised for the relief of obstruction following operation, in cases of long standing acute obstruction from some unknown cause, and for nutritive purposes in cases of widespread cancer of the stomach obstructing the cardia and leaving little

room for gastrostomy, cases of extensive laceration of a cancer of the stomach made accidentally during exploration, and extreme cases of nervous vomiting of girls from 18 to 25 years of age. The operation for purposes of nutrition is performed through a midline or left lateral incision; for the relief of obstruction it is best to re-open the former incision unless it is infected. In obstruction cases the operation should be performed as soon as the evening of the third day or on the fourth day. If there is no general peritonitis and the obstructive condition is recognized early, the operator may explore the region of the primary operation, separating bands of adhesions or kinks and relieving the obstruction. If jejunostomy is considered necessary, a No. 10 English catheter is inserted a few inches into the lining of the selected gut and fixed to the bowel by a purse-string suture of chromic catgut or silk. The catheter is then depressed into the wall of the bowel, which is sutured over it for an inch and a half. It is passed through a perforation in the omentum and brought out through the incision, sutures being passed through the peritoneum, the omentum, and the intestine on each side of the tube. In the larger number of a series of 43 cases the operation was necessitated by cancer, and was palliative. Twelve of the patients died within a week, and 4 more within a month, but in all cases the operation served its purpose of affording temporary or permanent relief. C. H. Mayo (Journal-Lancet, Dec. 15, 1917).

Surgery of the Appendix.—The vermiform appendix, while nominally a portion of the colon, is subject to peculiar affections which, in themselves often trivial, are prone to give rise to the most serious surgical complications. The mere removal of the appendix makes up a small portion of the actual surgery of this organ, which includes the surgical management of appendix-abscesses, appendix-peritonitis, and other complications. Hence the description of appendectomy as a typical operation representing the surgery of the organ is a small part of the subject, and requires elaboration only because of the different complications surrounding the work.

The typical operation in a case of early infection, or in fibroid degeneration of the appendix, consists in bringing the appendix to the outside of the abdomen, ligating it like an artery with catgut at two points, one-fourth inch apart. We sever the appendix between these two points of ligation and carry a drop of 95 per cent. carbolic acid into the lumen of each stump. The scissors or knife with which the severing is done is not used again at the operation, because the instrument is now infected, and is to be put aside in a safe place. The carbolic acid has sterilized the tissues with which it has come in contact instantly, and in order to stop any further and undesirable action we neutralize the carbolic acid with a few drops of alcohol applied with a pledget of cotton.

The next step is ligation of the mesappendix with catgut at as many points as desirable in any particular case. In some cases the mesappendix allows a safe ligation with a single ligature. In other cases where it has a particularly broad attachment, four or five ligatures may be required. It is quite as important in ligating mesappendix as in ligating broad ligament after an operation for ovariotomy, not to include too much tissue in any one ligature, and not to cut the stumps too short above the ligature, for the reason that vomiting and

other movements subsequent to the operation are particularly apt to force off these ligatures and give rise to secondary hemorrhage or opening of the lumen of the appendix. The last step after cutting away the mesappendix consists in scarifying the peritoneum of the cecum near the stump of the appendix that is left, with the point of a needle, in order to insure an abundance of lymph exudation which will wall in the stump.

The author has employed practically all of the fanciful methods of treatment of the stump which have been described by authors, and has dropped all but this simple method, which saves time. At one hospital where four thousand appendectomies performed by this method have been tabulated, there were only two cases of trouble due to the form of procedure, and both of these were due to the slipping of a ligature, both ligatures having been tied by the same member of the house staff, who may not have learned to tie square knots, or who may have cut stumps too short. Where old adhesions make it difficult to bring the appendix out upon the abdominal wall, this simple method of treatment of the stump does away with many difficulties.

In cases of acute infection with abscess, with dense new or old adhesions, it is extremely unwise to attempt to bring the cecum to the surface in order to carry out peculiar methods of treatment of the stump of the appendix, and in such cases it will suffice if we snap a pair of forceps upon the appendix close to the cecum, and remove the appendix with the finger without further detail, unless one wishes to leave another pair of forceps on the mesappendix. The

forceps left in place for twenty-four hours serve to protect also the small drain placed alongside. At the end of twenty-four hours the forceps may be removed, and no more attention given to the stump of the appendix. In these far-advanced cases the arteries of the mesappendix have commonly been occluded by proliferating endarteritis and the veins are filled with thrombi, so that the hemorrhage amounts to nothing more than a moderate degree of oozing cared for by the capillary drain. Such simple treatment does away with a great part of the dangerously severe part of operative work which in the third era of surgery has often been thought necessary. Treatment of abscesses and peritonitis of appendix origin is discussed under the general head elsewhere in the article. See also APPENDICOSTOMY and the article on APPENDICITIS in the second volume of this work.

Analysis of 822 cases of appendiceal operation at the Cook County Hospital, Chicago, between November, 1912, and February, 1916. Of the 58 terminating in death, 17 showed general peritonitis at the time of operation, and should be considered as cases of general peritonitis. Deducting them from the 58, the mortality is 4.98 per cent. for uncomplicated acute appendicitis. Of 445 patients operated on for simple acute appendicitis, 5 died, a mortality of a trifle over 1 per cent. Of 266 patients operated on for acute appendicitis—suppurative, gangrenous, perforating—with abscess, 6 died, a mortality of 2.2 per cent. Of 127 patients having gangrenous appendicitis without abscess formation; 7 died, a mortality of 5.5 per cent. Of the series, 150 cases occurred in children under 15 years of age. Of these, 138 recovered and 12 died, a mortality of 8 per cent. The following conclusions are drawn:

General peritonitis is still the most frequent complication of acute appendicitis. Drainage tubes, gauze, etc., should be removed gradually to avoid inclusions and subsequent spread of infection. Early operation means a low mortality. Abscess formation may be considered evidence of resisting power on the part of the organism. Fecal fistula, while comparatively frequent and annoying, has little importance in increasing mortality. Abortion is not greatly to be feared if appendicitis occurs during pregnancy. P. F. Morf (Jour. Amer. Med. Assoc., lxviii, 902, 1917).

Report on local anesthesia in 60 operations for acute and chronic appendicitis. Three-quarters of an hour before operation ¼ grain (0.016 Gm.) of **morphine** is given hypodermatically, and usually repeated just before operation unless the patient is drowsy. A 1 per cent. **novocaine** (procaine) solution is used, to the ounce of which 20 drops of 1:1000 solution of **epinephrin** are added. The meso-appendix is injected as well as the wall layers. There was no mortality. The average time of operation was 22 minutes, the length of time being due to the waiting for action of the anesthetic on the separate abdominal layers and mesenteriolum. Postoperative distention was usually absent. The day following operation, the author gives **pituitrin** 1 c.c. (16 minims), and one-half hour later a rectal irrigation or high enema. The average stay in bed was less than 7 days. The chronic cases usually left the hospital 2 or 3 days later. Recent adhesions could be separated without pain; when dense, novocaine was injected. J. Wiener (N. Y. Med. Jour., Aug. 2, 1917).

In single suture appendicectomy, advised by the author in pelvic operations, the tip of the appendix is picked up in a clamp, and a long 16- to 18- inch suture carried through the clear triangular space at its base and tied, thus ligating the appendicular artery. The mesentery is then cut free, leaving a small stump. Continuous with the appendix, at its base, is the longitudinal stria of the cecum. One-fourth of an inch from this base the needle is carried with a Lembert-Czerny stitch as a fixation suture to prevent the ligature from slipping. The needle is now carried back and inserted through the mesentery between the first ligature and the base of the appendix, and tied to the proximal end of the first knot. The appendix is clamped, cut, and the stump treated with **carbolic acid** and **alcohol.** Anterior to the mesentery and upon the lower portion of the cecum, running in the direction of the ileum, there is always a fascial fold, the fold of Treves. This is now picked up on the needle and carried over to the most dependent portion of the cecum, where it is fixed with a Lembert-Czerny suture and tied. This covers the stump of the appendix and completes the operation, requiring in all 5 or 6 minutes' time. A. Walscheid (N. Y. Med. Jour., cvii, 8, 1918).

Reviewing the opinions of surgeons on Lane's theories as to the causation of intestinal stasis, and the results thereof, the writer concludes that although there is certainly an element of truth in Lane's theories and practice, his operative procedures were altogether too radical. In his opinion surgery of the large intestine must be limited, with few exceptions, to cases showing definite evidence of obstruction. Ileosigmoidostomy should be cast aside as an operation of election, resection being the ideal procedure. In fact Lane is said to have discarded ileosigmoidostomy in favor of resection. Side by side anastomoses are unsatisfactory, as demonstrated by the frequency with which diverticula developed in the blind end. End-to-end anastomosis gives the most satisfactory results. G. L. McGuire (Trans. Can. Med. Assoc.; N. Y. Med. Jour., July 13, 1918).

Colostomy.—Now and then it becomes necessary to perform colostomy

for patients suffering from chronic obstruction induced by a growth, stricture, angulation, adhesion, volvulus, invagination, foreign body, diverticulum, or enteroptosis, after other measures have been tried and failed. Again, an artificial anus is sometimes made to relieve patients suffering from membranous catarrh, the various types of ulcerative colitis and multiple polypi, but this procedure is not so popular for this purpose as it was before the advent of appendicostomy and cecostomy.

An artificial anus should never be made except as a *dernier ressort* because of its unnatural location, the odors which emanate from it, the necessity of wearing a bandage, and, further, because a serious operation is required when the time for its closure arrives.

An artificial anus may be temporary when made as a preliminary step to excision and resection or until such time as the condition, for the relief of which it was made, has been cured; or permanent, when the opening is to remain through life.

It is not necessary to spend as much time in the formation of a temporary anus as it is in the making of a permanent anus, because the former is to be of short duration and the patient can bear the annoyance for a short time. In permanent colostomy it is of the utmost importance to provide for the patient's comfort by making the opening in such a way as to avoid painful evacuations, complete fecal incontinence or procidentia.

Formerly there was considerable discussion as to which was the better procedure, inguinal or lumbar colostomy; but lately the latter has fallen completely into disuse because the operation is more difficult, a suitable spur cannot be made, and the anus is situated where the patient cannot easily attend to it, while the former operation is devoid of all of these disadvantages.

Except where there are special reasons for doing otherwise, the colonic aperture should be made of fair size and as low down in the bowel as possible, because here the feces are more solid and give less trouble than when the anus is established at or near the cecum. An anal opening should never be made in the small bowel because when this is done there is a constant discharge of fluid through it, which annoys the patient and keeps the skin continually excoriated.

The majority of surgeons concentrate their efforts toward the formation of a proper spur and the production of the double-barrel-gun effect, to prevent any of the feces from reaching the rectum, but do comparatively little toward providing an anus over which the patient can exert a fair degree of control.

Gant's Colostomy.—The sigmoid is reached and isolated through a two-inch incision which crosses a line extending from the umbilicus to the anterior superior spine of the ileum, at the inner border of the oblique muscles; working outward, the transversalis is separated from the internal oblique muscle, with the index and middle fingers, for about one and one-half inches. The fingers are then forced upward through the oblique muscles and then over the external oblique and inward to the incision, separating the subcutaneous fat from the muscle. A loop of the sigmoid is now hooked up and then made to traverse the

route taken by the fingers, which makes it pass outward between the internal oblique and the transversalis muscles, and then through the internal and external obliques and finally over the latter back to the incision. Again, when it is sutured after being made taut to avoid the possibility of subsequent procidentia, the angles of the wound are approximated by two chromicized catgut sutures, which pass through the skin and fascia on one side of the incision and then beneath the longitudinal band of the sigmoid and out through the same structures on the other side, where they are tied. After the gut has been attached to the skin by a few plain catgut sutures it is surrounded by a bird's nest dressing to prevent its being pressed upon, covered with rubber tissue lubricated with sterile vaselin to prevent sticking of the gauze to the bowel, and then the outer dressing and binder are applied.

The intestine is not opened until after the third day, except when there is a marked distention; under such circumstances it is punctured at any time after six hours and amputated later. The projecting piece of gut is quickly and painlessly removed by injecting a small quantity of a one-eighth per cent. eucain solution into its mesentery. Cutting of the bowel proper causes no pain and does not require anesthetizing.

By a few cuts of the scissors, the intestine is amputated about one-quarter of an inch from the skin, bleeding points are ligated *en masse,* and hemorrhage from oozing surfaces is controlled by hot-water compresses or the cautery. The raw edges left are encouraged to heal rapidly by the occasional application of 6 per cent. **silver nitrate.** When the obstruction is located above the sigmoid, the steps in the operation must necessarily be modified to meet the indications, but the changes in the technique will suggest themselves to the surgeon in individual cases.

Patients have but little control over an artificial anus for the first few days, no matter what operation is performed, because the soreness of the wound and the irritability of the intestine excite frequent and strong peristalsis and the involuntary discharge of the feces.

This procedure has the advantage over other colostomies in that but one incision is made and, further, because it gives the patient a more perfect control over the movements than do other colostomies.

According to Gant, patients operated upon in this way except during the first few days rarely complain of the involuntary escape of gas and ordinarily do not have an evacuation until they have taken a mild laxative or stimulated peristalsis by a small enema.

It requires very little time to perform colostomy for a patient and the operation is practically devoid of danger, but the reverse obtains in the operation for its closure, as usually done by intestinal anastomosis.

To avoid the dangers which accompany joining of the two ends of gut, Gant has devised a special plan for closing artificial ani. Some years ago he invented a clamp, which has proved useful in the closing of colostomy openings. Its weight is imperceptible to the patient, and when in place the shank, which is bent at an angle to the clamp, lies flat upon the

abdomen. The jaws are fenestrated, one-half inch broad and one and one-fourth inches in length. It is applied as follows: The clamp is placed in the applicator forceps, which are so adjusted that the jaws of the clamp remain open to the fullest extent. The parts having been cleansed, the partition between the upper and lower colostomy openings is stripped to dislodge any coil of the intestine which might otherwise be injured.

The writer describes the following method calculated to insure sphincteric control after colostomy: The rectus is split vertically and the sigmoid is drawn out and divided at a convenient point. The lower segment is closed and replaced in the abdomen. The upper segment is made less bulky by removing the appendices epiploicæ and freeing it of mesenteric fat, but without in any way interfering with its blood-supply. The artificial sphincter is then made in the following manner: A loop of muscle-fibers is separated
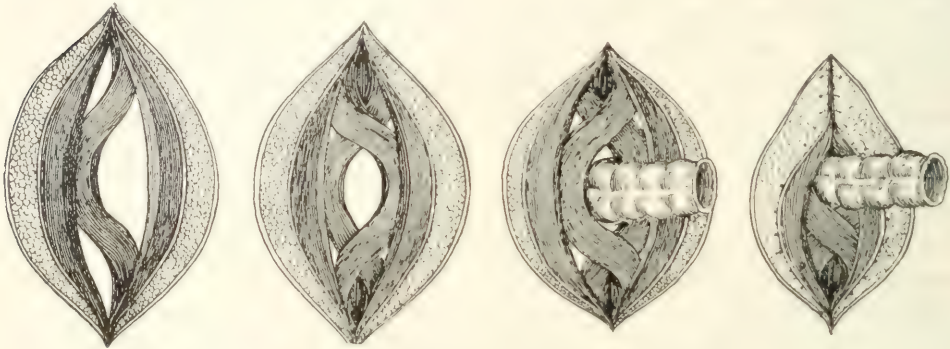
Operation for sphincter control after colostomy. (*Ryall.*)
(Clinical Journal.)

The clamp is then applied, one blade in each opening, and pushed down sufficiently to include the entire spur, when it is released from the instrument. It is allowed to remain *in situ* until the spur is divided and it comes away unaided, which is usually from six to nine days later. The clamp causes slight soreness, but no acute pain. To avoid complications, the patient had best remain quietly in bed until it sloughs out. When the partition has been successfully destroyed the skin and edges of the opening are freshened under local anesthesia and closed with catgut or silk, and, in case there is considerable tension, the wound is supported by well-adjusted adhesive straps.

from the posterior aspect of the rectus on either side of the wound. Each loop is then drawn over to the opposite side of the wound, so that one loop overlaps the other. The overlapping loops thus form a ring and through this the bowel segment is drawn. Sutures are then inserted to keep the muscle-fibers together above and below where the bowel comes through. Anchoring stitches are inserted through the skin and muscle inside to keep the bowel in position. The wound is then closed above and below the bowel, and the cut edges of the latter are sutured to the skin. A double sphincter is thus formed consisting of longitudinal and circular fibers. The longitudinal fibers are those of the anterior portion of the rectus, and the circular fibers are formed by the loops from the posterior part of the rectus. This operation can be modified by making double loops on each side and making them overlap one

another alternately. A similar operation can be, and has been, carried through the external oblique, and likewise can be done wherever the bowel is brought through muscle. A somewhat similar operation can be performed for gastrostomy and appendicostomy. C. Ryall (Clinical Journal, Nov. 11, 1908).

Lilienthal's Colostomy.—The formation of an artificial anus for the permanent relief of obstruction of the lower bowel is regarded by most surgeons as a loathsome makeshift for the prolongation of life. The mental picture of such an opening suggests the constant uncontrollable discharge of feces and flatus, the painful and annoying dermatitis in the neighborhood of the exposed mucosa, and the necessity for constant change of dressings—in short, a condition of actual and permanent disability for the ordinary duties and pleasures of life.

For a number of years Lilienthal has been performing an operation which obviates nearly all the discomfort and filthiness of colostomy. The patients have absolute control of the bowels and can even hold a considerable quantity of fluid injected into the colon. The bowels move once or twice a day, the patient knows when the movements are about to occur, and—not by any means the least advantage—he is not annoyed by the necessity for wearing an appliance for obturation. The operation has been tested many times, and the patients have been for the most part carefully followed up. A description of the steps of the operation follows:—

An incision about 3½ inches long, more or less, is made over the outer third of the left rectus muscle and parallel with its fibers. The upper end of this incision is just about on a line between the umbilicus and the left an-

terior superior iliac spine, but the exact length and location of the wound depends somewhat on the amount of subcutaneous fat present. Through this incision the fingers explore the abdominal organs and the type and limitations of the stricture or tumor are learned. The sigmoid flexure, be it well developed or not, is drawn out. As is well known, this part of the intestine varies greatly in length, but all is taken out which can be withdrawn without tension. The two legs of the loop are separated as widely as possible, the upper leg being sutured to the peritoneum and posterior rectus sheath in the upper angle of the wound, and the lower is sutured in a similar manner to the inferior angle. Silk or linen thread is the suture material, and the stitching is done by the continuous method, every third stitch being tied so as to avoid purse-stringing. The mesosigmoid is now sutured through and through to the peritoneum on each side (Fig. 1 in the annexed plates).

At the lower leg of the loop the gut is doubly ligated very tightly with heavy silk or cotton twine. Section is carefully made between the ligatures, taking care to avoid soiling from the small amount of imprisoned intestinal contents. Pure carbolic acid on a gauze sponge is used to sterilize the mucosa. Chain ligatures of catgut or silk are now passed through the mesosigmoid so as to prevent hemorrhage, and this membrane is then cut across. We now have a short piece of sigmoid, the distal leg of the loop in the lower angle of the wound, and a long piece sutured in the upper angle of the wound. The remainder of the mesosigmoid is cut away from the long piece of intestine, freeing it completely. The entire wound is now protected by gauze pack-

ings, the peritoneum by our previous procedures being entirely closed off by suture. We should have about 3 or 4 inches of free sigmoid at the upper angle of the wound. If there is more it should be ablated. Four equidistant clamps are now placed at the edge of this upper piece of intestine; the gloved finger is inserted into the lumen of the gut to the place where it is held to the peritoneum by suture; an assistant rotates the clamps so as to twist the gut around its longitudinal axis, after the manner described by Gersuny, from 180 to 360 degrees according to the texture and thickness of the walls of the sigmoid with which we are working. By withdrawing and reinserting the finger from time to time the degree of constriction which this maneuver produces may be accurately gauged. When this seems to be sufficient for the purpose—a matter of individual judgment—a few interrupted silk or linen sutures passed through the visceral peritoneum and submucosa to the aponeurosis of the external oblique hold the rotated gut in position. It is now necessary to make sure by re-examination that a sufficient twist has been accomplished. If this seems satisfactory more sutures should be put in to hold the gut firmly to the aponeurosis.

In examining with the finger now we find a double sphincter, the first one at the twist; the second, more an angulation than a sphincter, at the point of peritoneal fixation. A few chromic gut sutures close the portion of the remaining wound in the aponeurosis. The sphincteric action is maintaned by the fibers of the rectus muscle as well as by the twist in the intestine. A large-sized, rather stiff-walled rubber rectal tube, not a woven

one, is now inserted about six inches into the intestine and is tied in place, a single light suture passing through its walls guarding against its accidental extrusion. The remainder of the wound is left open and packed with gauze while the tube is led off into a receptacle at the side of the bed. These wounds always become more or less infected, but I have encountered a true phlegmon only once and then a single incision sufficed for its drainage.

About a week after the operation the tube may be withdrawn and the redundant sigmoid burned off with the actual cautery. Anesthesia is not necessary. Even then it will be found that repeated cauterizations will be required during the course of the healing in order to bring the intestinal mucosa to the skin level. Daily irrigations through the tube should be practised so as to keep the patient's bowels open. The string around the lower piece of intestine should be removed in three or four days; otherwise, there might be danger of complete and permanent closure, and it is necessary to maintain patency here for the sake of drainage.

The control of the bowels is learned gradually by the patient, and he is assisted by a constipating diet and, for the first few weeks, small doses of deodorized tincture of opium and of subgallate of bismuth, 20 grains three to five times a day. It takes about a month for the final result to be attained, but the functional result in all uncomplicated cases will be found perfect.

The writer employs one of the following procedures: (1) Sigmoid above the stricture joined to the sound lower part of rectum; (2) if sigmoid fixed, transverse colon, if low, anastomosed to the rectum and
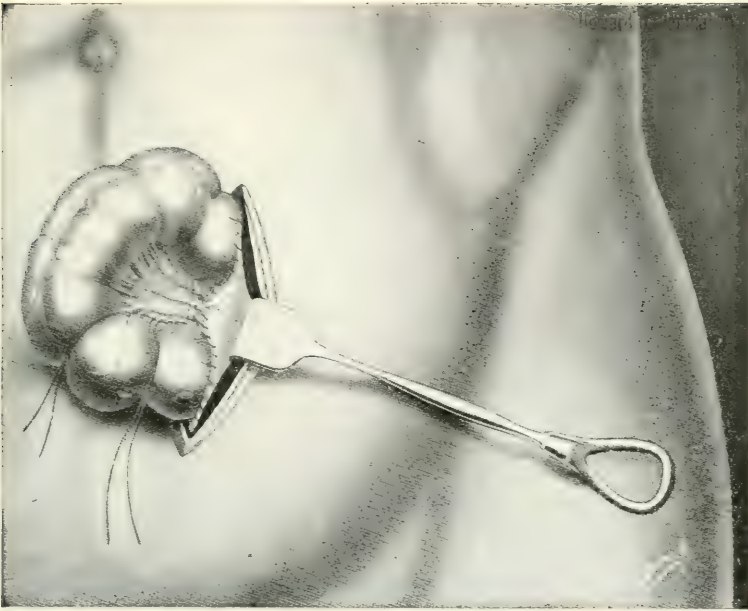
The Dotted Line Shows Line of Section. The Blunt Retractor
Holds Outer Third of Rectus Muscle Together with Skin
and Aponeurosis. (*Howard Lilienthal.*)
Annals of Surgery.
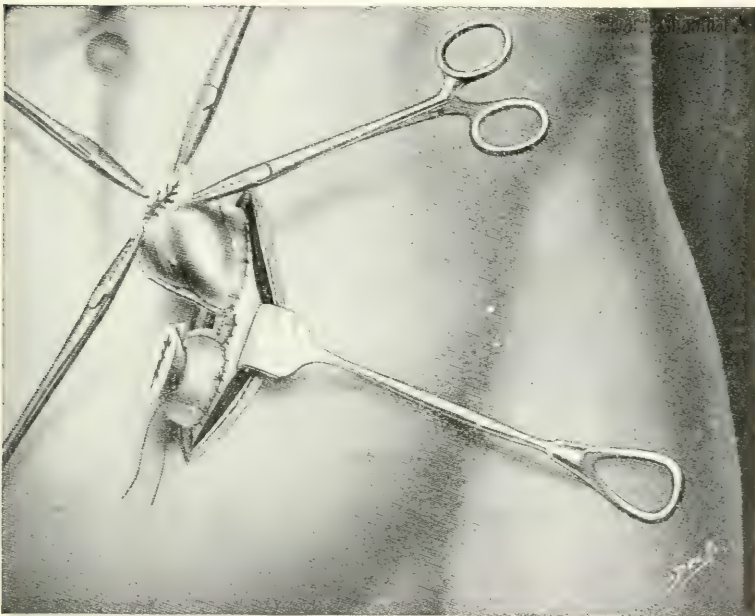
Redundant Bowel and Mesocolon Cut Away. Twisting of the
Intestine Begun. (*Howard Lilienthal.*)
Annals of Surgery.
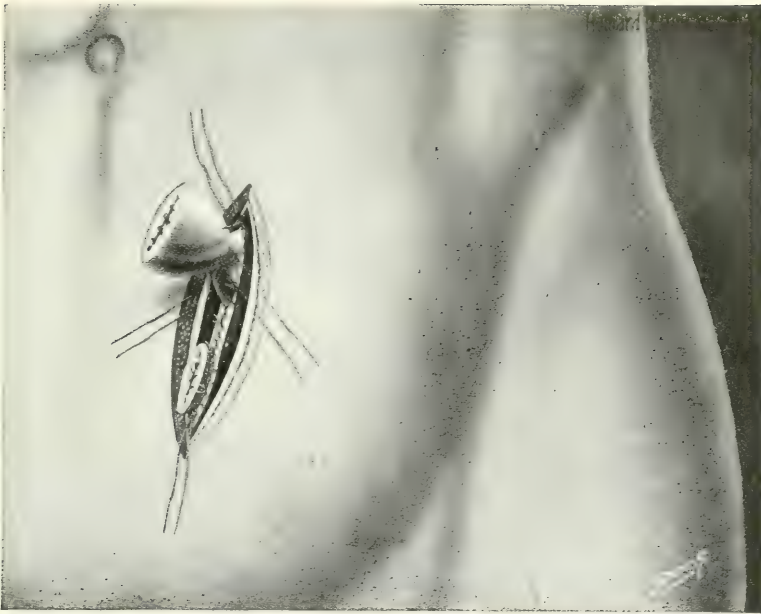
Twist Complete and Maintained in Position by Anchor Sutures
Holding Sigmoid to Aponeurosis. (*Howard Lilienthal.*)
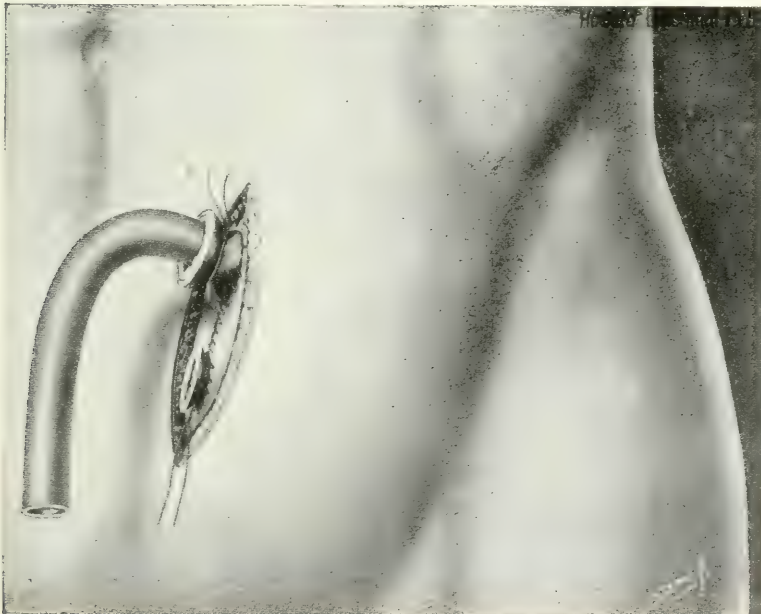
Operation Complete. Aponeurosis Further Stitched to Intestine
and Wound Closed with the Exception of the
Skin. (*Howard Lilienthal.*)

to the descending colon above stricture; (3) cecum joined to rectum and the ileum to colon above stricture; (4) lowest coil of ileum,joined to the rectum and by a lateral anastomosis to the descending colon above the obstruction.

In the upper opening the small female end of a Hildebrand button is inserted and fixed with a purse-string suture. With special forceps the larger male end is passed through the rectum and made to project upward, so that a small incision may be made over the central part, which then protrudes, allowing the bowel wall to slide down so close to the spring that no suture is needed. The 2 halves of the button are then clamped. The result is a passage for fecal matter into the rectum instead of outward on the abdomen. McArdle (Pract., June, 1916).

The indications for colostomy are given by the writer as follows: (1) As a preliminary to excision of the rectum for cancer. (2) To prolong life and prevent obstruction in inoperable cancer of the lower bowel. (3) In all cases of pericolitis of the lower part of the pelvic colon where resection or short-circuiting is impossible. (4) In some cases of intractable ulceration of the rectum. (5) In intractable fibrous stricture of the rectum. (6) As a temporary measure in severe wounds of the rectum.

Referring in particular to transverse colostomy, he points out certain advantages of this procedure. It seems to afford better control over the stools than sigmoid colostomy, and prolapse is much less common. In performing transverse colostomy, the colon should not be opened at the most dependent part but as near the splenic flexure as is possible without causing tension. When the transverse colon is short, sigmoid colostomy should be preferred. The colon should subsequently be cut completely in half to arrest the peristaltic wave at the opening. Lockhart-Mummery (Practitioner, Aug., 1917).

Appendicostomy and Cecostomy.— These operations are useful in the treatment of disease located in the colon, but, when the disturbance lies within the small bowel or involves it and the large intestine, Gant's cecostomy, which provides a means by which the treatment can be directly applied to both, should be substituted. It is frequently impossible to determine whether the disease is limited to the colon or not, and because of this and the fact that this operation is no more difficult or dangerous than appendicostomy and ordinary cecostomy, and is equally effective both when the lesions are located in the small intestine, the large bowel or both, Gant believes his to be the most desirable procedure.

Appendicostomy.—Some surgeons do not open the appendix during the operation because they fear infection. This practice, Gant believes, is bad except when it is obvious that the appendix is not obstructed, because he has encountered three failures following it; in one the appendix was too short, in another it was strictured, and in still another it was blocked by an encysted grapeseed.

He immediately amputates the appendix and introduces the probe-pointed appendiceal irrigator, then nothing can interfere with postoperative irrigation, but when the appendix is diseased it is removed and cecostomy is performed. It is important that the irrigations be started at once when patients suffering from ulcerative colitis are despondent, greatly debilitated, have many movements, lose considerable blood, and suffer from insomnia and autointoxication.

To meet these conditions Gant has

devised a technique for appendicos-
tomy which provides for irrigation
both during and following the opera-
tion, since the adoption of which his
patients have gained very much more
rapidly than formerly, when the ap-
pendix was not opened for several
days, during which time nothing was
done to relieve them. Now and then
a stitch abscess has occurred, but
other complications have not arisen
during or following the operation.
Briefly described, the following are
the steps: 1. The appendix is ap-
proached through a gridiron incision
and located by tracing the anterior
longitudinal band downward, when it
and the cecum are freed and brought
outside. 2. The cecum is drawn first
to one side and then the other by an
assistant, while the parietal perito-
neum is removed at the sides of the
incision to insure union between it
and the transversalis fascia, or the
peritoneum is left intact when the
gut is to be brought into contact with
it. 3. The appendix is freed and
straightened by ligating and dividing
adhesions and the mesentery at about
one-fourth inch from it. 4. After the
cecum has been scarified, two sero-
muscular suspensory sutures are in-
troduced on either side and near the
base of the appendix, each taking
three bites in the gut. 5. By means
of a strong, long-handled needle, the
anchoring stitches are in turn carried
through the entire thickness of the
abdomen and clamped with forceps,
but when the intestine is joined
directly to the peritoneum the bowel
is anchored by chromicized gut su-
tures, including the parietal perito-
neum and transversalis fascia. 6.
Having surrounded the appendix with
gauze, a traction suture is introduced

to steady it while it is being ampu-
tated, cauterized, and probed. 7. A
Gant appendiceal irrigator closed with
a stopper is introduced and the ap-
pendix ligated above it. 8. The ap-
pendix is placed in the lower angle
of the wound, pointing upward to
prevent leakage later, and anchored
by two seromuscular chromicized-gut
sutures, which include the trans-
versalis fascia. 9. The abdominal
layers are then separately approxi-
mated by interrupted or continuous
stitches, after which the cecal sus-
pensory sutures are tied across rubber
tubes. 10. The appendiceal irrigator
is prevented from slipping out by the
adjustment of adhesive straps or by
means of attached pieces of tape
which encircle the body. 11. In
urgent cases from one to three pints
of warm **saline solution** are imme-
diately injected into the colon, when
the stopper is introduced to prevent
leakage. 12. The wound is sealed by
means of cotton and collodion, and is
protected further by split gauze pads
which overlap each other when placed
about the appendix. 13. The outer
end of the irrigator is surrounded by
twisted gauze strips to prevent pres-
sure upon it when the outer dressings
composed of gauze pads or cotton and
a many-tailed binder are adjusted.

In gastro-intestinal perforation fol-
lowed by acute peritonitis, the writer
noted that the nausea, vomiting, and
cardiac and pulmonary symptoms
due to paralysis of the intestine,
cease after appendicostomy, normal
peristalsis being, moreover, re-estab-
lished. The fluid introduced through
the appendix by the drop method is
quickly absorbed and nothing need
be given by mouth until normal con-
ditions are restored in the intestine.
After 12 hours, the fluid discharged by
rectum is usually colored with bile,

showing intestinal paresis has been overcome. Appendicostomy does not prolong the major operation more than 2 or 3 minutes. The absorption of water prevents shock and causes rapid detoxication by washing out the large intestine; siphonage of the small bowel is also effected. The writer reports 10 cases, in 1 of which the bowel had been perforated in 8 places by a bullet. Two patients had been run over. Most of the other cases were perforated gastric ulcers. The appendicostomy gave results not obtainable by any other procedure. J. Roux (Rev. méd. de la Suisse Rom., xxxv, 814, 1915).

Appendicostomy has the advantage over cecostomy in that there is no discharge of feces or gas. A woman who had suffered over 14 months from bloody diarrhea was sent to a hospital with a diagnosis of tuberculosis of the intestines. An exploratory laparotomy having disproved this, and colitis been found, appendicostomy was performed. **Enemas of salt solution** were then given by the drop method, and later drop enemas of 1 to 2 per cent. **tannin solution** 3 times daily. There was prompt improvement and after 2 months complete recovery. The drop enemas were continued by the patient herself. After a recurrence from neglect the fistula was dilated with a laminaria tent and the treatment resumed. The patient then recovered completely. Hans Brossmann (Med. Klinik, Sept. 1, 1921).

Appendicocecostomy.—On a number of occasions Gant has been compelled to abandon appendicostomy for cecostomy because the appendix was too short, strictured, or blocked by a grapeseed which rendered it unfit for irrigating purposes or had sloughed off following appendicostomy. In each instance, after the appendix had been amputated or inverted, a catheter was introduced through the appendiceal stump or opening and fastened by a purse-string suture introduced at or near its base. The cecum was suspended and the rest of the operation performed as in appendicostomy.

Two patients suffered from diarrhea induced by ulcerative lesions in the colon. In these cases the catheter was introduced a short way into the cecum, providing for colonic irrigation. The others were afflicted with enterocolitis, and it was thought advisable to irrigate both the large and small intestines. This was accomplished by guiding a catheter across the cecum through the ileocecal valve into the small bowel. This procedure is termed "appendicocecostomy."

The principal objections to this operation are (1) that a change of catheters is impossible because the appendiceal and ileocecal openings are nearly on the same level, and (2) because the appendiceal aperture is so small that two catheters of sufficient size cannot be introduced to provide for large and small bowel irrigation.

Cecostomy.—Experience has demonstrated to Gant's satisfaction that cecostomy is preferable to appendicostomy in the direct treating of intestinal disease. A comparative study of the advantages of cecostomy and the disadvantages of appendicostomy, as enumerated below, will show why the former should take preference over the latter.

The advantages of the cecostomy operation, and more especially the writer's cecostomy, which provides a means of irrigating both the large and small intestine, are: 1. Owing to the fact that the cecum lies against the inner abdominal parietes, it can be easily anchored without angulating

or twisting the bowel. 2. Since the opening is opposite the ileocecal valve, a catheter can be introduced into the small bowel for irrigating purposes or the siphoning of its contents for examination. 3. The cecal opening can invariably be made of a suitable size. 4. The circular, valve-like projection formed around the catheter by the infolding purse-string sutures prevents leakage. 5. The catheter can be changed without difficulty. 6. Closure of the opening follows withdrawal of the catheter and a few applications of the copper stick or cautery. 7. Owing to the natural position of the cecum, there is less tension and pain following its anchorage to the abdomen than occurs after appendicostomy. 8. This cecostomy may be employed in the treatment of lesions located anywhere in the intestinal canal, while appendicostomy is limited to those in the colon.

The disadvantages of appendicostomy are the following: 1. The appendix is more difficult to bring up for anchorage than the cecum because of its deeper and more uncertain position, and because it is frequently bound down by adhesions or a short mesentery. 2. Anchoring of the appendix causes angulation or twisting of the cecum, which, in turn, may induce constipation, discomfort, or pain. 3. When the cecum about the appendiceal base is caught in the wound, it induces nausea and vomiting until detached (writer's case). 4. When the appendix is small, short, strictured, bound down by adhesions, blocked, or is otherwise diseased, it is useless for irrigating purposes. 5. Irrigation is frequently difficult and unsatisfactory because of the small appendiceal opening. 6. Pain follow-

ing appendicostomy is much greater than after cecostomy owing to the pulling upon the appendix by the loaded cecum, the periappendiceal adhesions, or the squeezing of the attached mesentery when the wound is closed tightly about it. 7. Frequent dilatation or the insertion of a catheter is often necessary to keep the opening sufficiently large. 8. Death has followed injection of the irrigating fluid into the abdomen beside the appendix where an interne mistook an opening in the wound for that of the appendix. 9. After a cure it is more difficult to close the appendiceal than the cecal outlet, and frequently appendectomy is imperative. 10. Appendicostomy frequently fails because the appendix slips back into the abdomen or retracts sufficiently to make irrigation almost or quite impossible. 11. The appendix has been known to slough off on several occasions owing to tension, its constriction by the sutures or destruction of its blood-supply making subsequent cecostomy necessary. 12. Appendicostomy is not effective when the disease is located in the small intestine. 13. Appendicitis requiring appendectomy following closure of the appendiceal outlet has occurred. 14. Owing to the irritation caused by the catheter or treatment the mucosa may become so inflamed and swollen, ulcerated or strictured, that irrigation must be abandoned. 15. Finally, according to Reed, the catheter causes the wall of the appendix frequently to perish in a few days.

Cecostomy with an Arrangement for Irrigating both the Small Intestine and Colon.—Gant has described what he believes to be an original way of irrigating both the small and large bowel

through the same opening in the cecum—an operation which, for want of a better name, he has designated "cecostomy with an arrangement for irrigating both the small intestine and colon."

He believes his cecostomy is superior because the technique is simple, the operation requires no more time than others, there is less leakage owing to the purse-string infolding being substituted for his lateral sutures, both the small and large bowel can be irrigated by the attendant or patient, a firmer support is obtained by attaching the cecum to the transversalis fascia than to the parietal peritoneum, and the opening heals spontaneously after the catheters are removed.

Briefly described, the steps in Gant's cecostomy are: 1. Through a two-inch intermuscular incision made directly over the cecum, it and the lowermost part of the ileum are withdrawn and the edges of the wound covered with gauze handkerchiefs. 2. The anterior surface of the cecum is scarified after the ascending colon and ileum have been clamped to prevent soiling of the wound when the bowel is opened. 3. Four linen seromuscular purse-string sutures are introduced into the anterior wall of the cecum opposite the ileocecal valve, and the bowel is opened inside the suture line. 4. The gut is grasped at the juncture of the large and small intestines and held in such a way that the ileocecal valve rests between the thumb and fingers of the left hand. A Gant catheter guide is then passed directly across the cecum and through the ileocecal valve into the small intestine, aided by the thumb and fingers. 5. The

guide is held by an assistant while the obturator is removed and a catheter is introduced into the small bowel. It is then removed and the catheter firmly held in the small gut by an assistant until anchored to the cecum by catgut sutures to prevent its slipping out during the operation. 6. A short rubber tube three inches long is projected into the cecum for an inch or more and anchored beside the one in the small gut. 7. The infolding purse-string sutures are now tied, forming a cone-shaped valve above the catheters to prevent leakage of gas and feces. 8. After removal of the clamps, the cecum is scarified and anchored to the transversalis fascia, denuded of its peritoneum by through-and-through suspension sutures of linen, or by chromicized catgut stitches, including the fascia, when the two peritoneal surfaces are to be approximated. 9. The wound is closed by the layer method and the catheters are fastened by stitching or by encircling them with an adhesive strip to hold them together, and crossing this at a right angle with a second piece of plaster placed between the catheter to prevent their slipping out. 10. The ends of the catheters are closed with cravat clamps to prevent leakage, and the operation is completed by applying the dressings above the projecting tubes.

One catheter is left longer than the other or is identified in some way in order that the interne or nurse may know *which is in the large* and *which in the small intestine* when time for irrigation arrives. To avoid danger from infection treatment is not begun before the fifth day except when urgent.

The catheter may be readily changed by cutting the attached adhesive strips and withdrawing the one projecting into the cecum. Gant's catheter guide is then passed over the other into the small intestine, where it is retained until the old tube has been removed and a new one introduced. A second piece of catheter is then placed in the cecum and both are prevented from slipping out by adjusting fresh adhesive straps after the manner already described.

Before deciding upon the above technique Gant irrigated the small intestine by passing a glass or silver catheter through a cecal opening, past the ileocecal valve, into the small gut each time it was irrigated, but this practice was abandoned as impracticable because of the difficulty encountered in locating and passing the valve, and, further, because the patient could not irrigate himself in this way.

Gant has had no reason to suspect that peristalsis forced the catheter out of the small intestine into the cecum except in one of his first cecostomies, where the tube was cut short and projected only one inch beyond the ileocecal valve instead of several, as it should. He feels confident that the catheter remained in the small gut in his other cases because (a) water injected through the colonic pipe was evacuated much quicker than when it was deposited in the small bowel; (b) when a minute quantity of a 10 per cent. solution of methylene-blue was injected through the former, it appeared in the urine more quickly than when introduced through the catheter in the small gut, and (c) the catheter guide could be carried over the tube

in the small intestine and the latter could be removed and replaced with a new one at will, and, further, (d) fluid feces could be withdrawn more quickly and frequently through the pipe in the small intestine than through the colonic catheter.

To avoid possible expulsion of the catheter from the ileum, catheters made of silk, silver, glass, and soft rubber reinforced by an inner metal tubing which cannot be forced out of the bowel owing to their non-flexibility are employed. Only that portion of the latter projecting into the small bowel was reinforced, and as a result it served the desired purpose and caused but little irritation because it was soft and flexible. This cecostomy permits the attendant or the patient to irrigate the small and large intestines at will, and the fluid may be siphoned or allowed to escape through the anus and the catheter can be changed quickly as often as is necessary.

Enterocolonic Irrigator.—An instrument successfully employed by Gant a number of times in direct treatment of intestinal affections involving both the large and small intestines. It is made both of rubber and metal.

When it is in position, the attached inflating bag lies in the small intestine at or near the ileocecal valve, and when distended prevents the escape of the solution into the cecum, thereby enabling the attendant to accurately gauge the amount of fluid deposited in the small bowel and to retain it there as long as required. By means of this twin-tube irrigator, the small and large intestines can be quickly and scientifically flushed, singly or together, by the physician, nurse, or patient.

The steps in cecostomy, when the irrigator is employed, are similar to those already described when separate catheters are used, except that the Gant catheter guide is unnecessary and the apparatus is retained in position by attached pieces of tape which encircle the body.

Indications for Direct Bowel Treatment.—This form of treatment has a wide field of usefulness. Most physicians and surgeons appear to labor under the impression that it is limited to the colon and is indicated *only* in ulcerative lesions of the large bowel causing diarrhea.

Gant has called attention to the fact that this type of cecostomy is indicated in the treatment of intestinal parasites, enteritis, enterocolitis, and catarrhal, tuberculous, syphilitic, dysenteric and gonorrheal colitis; ordinary and pernicious anemia; the many manifestations dependent upon intestinal autointoxication, ptomain poisoning, diarrhea of adults and children, intestinal feeding, malnutrition, and following operations upon the mouth, throat, esophagus or stomach; in gastric stricture, ulcer, cancer and other disturbances where rest of the organ is indicated. Gant also called attention to the fact that by means of his cecostomy various intestinal diseases could be investigated, and that the procedure could be used to determine the amount and nature of the intestinal juices and discharges, the character of the feces, the action of salines and other cathartics injected directly into the small and large bowel, and the marked immediate vasomotor effect following hot and cold enteroclysis and many other interesting problems.

Gant has also pointed out the usefulness of appendicostomy and cecostomy as a means of drainage when the cecum or other part of the colon was excluded. He has also employed appendicostomy and cecostomy a number of times when operating for mechanical constipation where colitis was a complication, and also in the palliative treatment of obstipation where the patient declined to have the cause of the obstruction removed and yet suffered from marked autointoxication or recurring impaction.

Gant and Reed have also performed cecostomy once for the relief of septic peritonitis. The latter recorded a case of "defective flora" of the colon which was improved by the **injection of the needed bacteria** through a cecostomy opening, and called attention to its usefulness in the treatment of intussusception.

Following direct treatment, the condition of the patient becomes rapidly better and manifestations such as anemia and those induced by autointoxication rapidly disappear, and in cases of diarrhea the frequency of the stools generally diminishes and the amount of blood, pus, and mucous passed becomes markedly less.

The good results following the **irrigating treatment** are due mainly to the mechanical action of the fluid in cleansing and stimulating the ulcers and removing retained toxins, and not to its temperature or chemical contents. Solutions should always be employed at the bodily temperature or warmer because of their soothing effect upon the irritated bowel, and not cold or at a freezing point, as recommended by some authors, because when injected ice cold they excite enterospasm and cause much unnecessary suffering.

Briefly stated, the most reliable, stimulating, and soothing remedies to employ are **weak solutions of boric acid, quinine, formalin, hydrastis, krameria and soda, silver nitrate,** and those of a soothing nature are **kerosene, liquid paraffin** or **olive oil,** according to indications. The stimulating solutions are used stronger when ulceration is extensive and the oils warm when the gut is irritable.

Colectomy.—Excision of the colon is performed for malignant disease, including tuberculosis and gangrene, but in practice the operation, like colostomy, is confined to cecectomy and sigmoidectomy, unless the morbid process directly involves the transverse colon, where the hepatic or splenic flexure is usually the seat of the disease.

Of late, colectomy more or less extensive, has been practised for severe chronic intestinal stasis.

In colectomy for stasis the chief object is first to separate the evolutionary adhesions from the mesentery. The outer peritoneal aspects of the mesenteries should be left smooth. The ileum is divided usually within a few inches of its termination. The longer the small bowel remaining, the greater the increase in weight after colectomy; in stout patients shortening of the small intestine is of material advantage. The pelvic colon is drawn up from the pelvis and grasped with forceps about 2 inches above the level of the pelvic brim, and the end of the ileum attached directly to the cut end of the pelvic colon. The innermost row of sutures perforates all the coats of the bowel, and is of the button-hole type, while the outer rows secure only the peritoneal and muscular coats. Difficulty in anastomosis because of the difference in caliber is met by arranging the sutures so that each picks up a correspondingly greater portion of

the circumference of the pelvic colon than of the ileum. Finally, the cut edges of the mesentery of the ileum and pelvic colon are sutured together, care being taken to leave no raw surface. An esophageal tube is introduced through the rectum and ileocolic junction. Lane (Brit. Jour. of Surg., Apr., 1915).

Summarizing the final results of total colectomy for constipation: in only 6 of 12 cases operated could the result be considered entirely satisfactory. In all cases there was great improvement in the constipation for a time, to be followed in 4 by a gradual recurrence, though in some cases not as severe as before. In no case was there diarrhea of long standing, nor undue thirst. In 6 cases there was marked improvement in nutrition. On the whole, total colectomy is justifiable only in severe cases of obstructive constipation. The colectomy should be limited to the ascending colon and the middle of the transverse colon, with lateral anastomosis of the ileum into the transverse colon. J. G. Clark (Surg., Gynec. and Obstet., May, 1916).

In carefully selected patients with stasis who are toxic from their condition, the writer deems right-sided colectomy, with preservation of the omentum, justifiable. It gives as good results as general colectomy and has less primary and secondary danger. There is great variation in the length and size of the human intestine. The shortest, 8 feet, is the carnivorous type; the longest, 33 feet, the herbivorous type. End-to-end union of ileum to colon is a safe procedure. The closed end of the large bowel, being incorporated into the wound and brought through the peritoneum, into but not through the muscle, may be opened to serve as a gas vent should the necessity arise. In most cases constipation is improved, but the best results follow operations of necessity for tumor and obstruction. Among 262 resections of the large intestine for malignancy, 54 per cent. of those who recovered

were alive after 5 years, and 67.5 per cent. after three years. Among 235 cases in which the right half of the colon was resected for tumors, disease and stasis, the operative mortality was 12.5 per cent. Mayo (Jour. Amer. Med. Assoc., Sept. 9, 1916).

Right colectomy is followed by less unpleasant postoperative sequelæ than total colectomy or ileosigmoidostomy, and is fully as satisfactory in relieving stasis. Only such cases as have failed to be relieved by simpler measures are considered suitable for operation.

In a postoperative X-ray study of 9 cases made for the purpose of determining whether the absence of an ileocecal valve had any effect on the emptying of the small bowel, it was found that in no case was there any damming back in the ileum or any evidence of dilatation of this portion of the bowel.

The operation consisted in the removal of the last few inches of the ileum, cecocolon, and about a third of the transverse colon. In his earliest cases, he did not remove as much of the transverse colon as he did later, and postoperative X-ray examination shows redundancy and ptosis of this portion of the colon, although the functional result was perfect. P. P. Johnson (Boston Med. and Surg. Jour., clxxvi, 266, 1917).

The writer performed 15 total colectomies for constipation, with 1 death; and right colectomy for cancer in 9 cases, with 2 deaths; for tuberculosis in 11 cases, with no deaths. For constipation a right hemicolectomy (the cecum, ascending colon, and half of the transverse colon) is not so effective as a total colectomy. The operation only relieves more or less, in a proportion dependent on the condition of the other organs.

In the older total colectomy, the omentum was sacrificed. The writer holds that the omentum must be preserved. But a total colectomy leaves irremediable and persistent abdominal disturbances, and Pauchet after 10 years' experience now does a right colectomy with preservation of the whole omentum. V. Pauchet (Presse méd., Sept. 9, 1918).

Series of 19 operations in which the *right* colon was excised for relief of symptoms which were attributed to blocking of feces in the cecum. The immediate result of the operation showed that it could be done without undue risk: 20 cases reported by Mayo, 12 by Johnson, and this series of 19, without a mortality. It is, however, too serious to be undertaken except for very definite conditions of incurable partial obstruction. The indications for excision are dilatation of the cecum, extreme mobility, presence of adhesions in patients unrelieved by any palliative treatment and whose symptoms lead to chronic invalidism. Brewster (Annals of Surg., Aug., 1918).

Cecectomy.—This operation, while so named, is by no means limited to the cecum, for it is usually necessary to remove either the ascending colon or a portion of ileum or of both intestines together. Hence such intervention may be termed ileocolectomy, ascending colectomy, etc., according to the individual case.

The incision is made in the middle line, unless the diagnosis has been made so well that the operator can incise directly over the growth. As in all similar cases, the gut is mobilized, brought out and walled off with gauze, while it is emptied and clamped or held empty by assistants' fingers or tape. The technique differs little from that of enterectomy of the small bowel. The mesentery is tied off and then divided, the large bowel excised and the operation completed by restoring the continuity of the intestine. As the cecum and appendix have been sacrificed, it is necessary to secure an anastomosis

between the ileum and transverse or descending colon.

An end-to-end anastomosis is hardly practicable because of the disparity in size between the small and large bowel. Hence a lateral anastomosis or an implantation is indicated, which may be made by suture or button. The technique is that usually pursued in all intestinal anastomoses.

Lateral anastomoses are practicable when the ileum is to be united with the neighboring ascending colon.

No attempt is made to provide for a cecal pouch or ileocecal valve, but the two ends are joined after the cut end of the colon has been closed.

It is sometimes advisable to implant the ileum in the descending colon or sigmoid flexure (ileosigmoidostomy). This would be necessary if the ascending colon were sacrificed.

Sigmoidectomy.—As the sigmoid flexure is a favorite seat for cancerous growths it is often necessary to excise this portion of the bowel. In some cases no attempt is made to restore the continuity of the bowel, but the operation is terminated by forming an artificial anus. If, however, the sigmoid is movable and the tumor can be removed cleanly, an end-to-end anastomosis may be made. Even when the rectum needs removal with the sigmoid, operators have preferred to draw down the sound intestine and suture it to the anal region.

In transperitoneal sigmoidotomy the author seldom uses the exaggerated Trendelenburg posture, and in old and adipose persons is especially cautious. The sigmoid is opened on the anterior longitudinal band and the tumor exposed, drawn through, and double clamped. The growth is removed with the cautery and the defect closed from the mucous side by continuous sutures of chromic catgut

after the method devised by Pilcher for the excision of hemorrhoids. It is covered on the peritoneal side with a few interrupted silk sutures. The incision in the sigmoid is then closed with continuous catgut and interrupted fine silk. A red rubber tube is now passed up into the sigmoid beyond the line of sutures and fastened with a catgut suture to the anus; this is left *in situ* for a few days to prevent gas pressure. The procedure described was found most efficient for growths similar to papilloma. Mayo (Annals of Surg., July, 1917).

In performing a three-stage operation for cancer of the sigmoid, the writer at the first operation draws the loop of bowel containing the growth out of the wound as far as possible and keeps it there by a glass rod passed through the mesocolon or by a couple of stitches. Delivery of the colon is often facilitated by division of the external mesocolon. A glass tube is tied into the loop above the growth either at the operation or 36 hours later. After 10 days, the part of the loop external to the abdominal wall is cut off, generally without an anesthetic. There is no pain except some colic if the mesocolon is ligated. The final operation can be performed at any time after the wound has healed. In 2 out of 3 cases the writer made end-to-end anastomoses in the abdominal wall without opening the peritoneal cavity. P. Lockhart-Mummery (Proctol. and Gastroenterol., xi, 80, 1917).

SURGICAL AFFECTIONS OF THE PANCREAS.—These comprise inflammation, cancer, cysts and calculi. There are no typical operations for these affections, or upon the pancreas and its duct for any conditions.

Acute Pancreatitis.—In this condition the pancreatic juice escapes into the tissues of the pancreas and into the peritoneal cavity, and the effect of its irritating influence is very de-

structive. The reddish, purulent fluid in the vicinity can be removed by a drain, and tense parts of the pancreas can be scarified to allow some of the interstitial exudates of the pancreas to drain out. Drainage is essential after removing tumors, or after an injury to the pancreas in order to dispose of the irritating pancreatic secretion.

The escape of pancreatic secretion from an injured gland reduces living fat in this vicinity into its fatty acid and glycerin, due to a ferment in the pancreatic fluid. The glycerin is absorbed and the fatty acid which remains makes a combination with lime salts, with the effect of producing small areas of dull white at points where the reaction has taken place.

Acute pancreatitis should be the occasion for prompt abdominal section for the severe and fulminating symptoms usually present, and emergency laparotomy would in any case be required. If the patients have not died outright of collapse or peritonitis, the fat necrosis or some other secondary conditon will demand operation.

> In the ultra-acute and acute varieties of pancreatitis immediate operation should be the rule, the prime object being early and adequate drainage. The best approach in this stage is by an anterior incision either through the gastrocolic omentum or the gastrohepatic ligament, depending on whether the stomach is situated high or low. The pancreas should be freely incised longitudinally, or numerous blunt punctures made in its substance, thus giving vent to the blood, lymph, and obstructed secretions. Both gauze and tube drainage should be laid down to the surface of the organ and conducted to the surface through a sheet of rubber dam to minimize adhesions. The only ex-

ceptions to the rule of immediate operation are severe shock and obvious improvement from the effects of the disease.

> In 13 operations for acute pancreatitis, 3 cases resulted fatally; one of these was of the ultra-acute variety. Usually there is ample margin of safety for the experienced abdominal surgeon also to open, empty, and drain the gall-bladder and common duct if necessary. J. B. Deaver (Jour. Amer. Med. Assoc., lxix, 434, 1917).

The pancreas may be reached either above or below the stomach, through a second incision into the omentum or mesocolon, after making a suitable external incision. A counteropening through the lumbar region may be necessary for drainage. If an abscess is still intact it should be opened wherever most accessible. The infrequently, fatal character, and operative mortality (chiefly unavoidable) do not justify us in devoting much space to abscess of the pancreas, the treatment of which largely resolves itself into management of the secondary conditions to which it gives rise. Shallow incisions followed by simple wick drainage carried to the pancreas certainly serve to remove poisonous exudates to advantage in some cases of acute pancreatitis, and even the simple use of wick drains without scarification of the pancreas is sometimes followed by good results. We must leave room when draining to allow necrotic masses to escape.

> Pancreatitis is, with few exceptions, an infective disorder, propagated in the majority of instances from the duodenum and gall-bladder, usually by the way of the lymphatics. Acute pancreatitis is usually infection plus ferment activity, though it may be traumatic or clinical exceptionally. In operating for acute pancreatitis, the diagnosis of pancreatitis is a

clinical inference based on the fact that pancreatic disease is associated with biliary disease in from 10 to 30 per cent. of all cases, that it is more often present with long-standing disease and with common duct involvement than with purely cholecystic inflammations.

Free drainage of the pancreas is a desideratum. The peritoneum over the organ should be scarified so that gauze drainage may be brought into direct contact with the surface. A large aspirating syringe will detect collections of fluid, and these should be opened freely. Peripancreatic collections sometimes form in the lesser sac and point in the left loin, where they may be evacuated. Abscesses presenting anteriorly rarely adhere to the parietal peritoneum, and must be evacuated transperitoneally, sometimes by a two-stage operation. Resulting sinuses are occasionally troublesome, the effects of the ferments evidencing themselves in the irritation of the skin. A strict anti-diabetic diet and bland ointments to the skin are helpful.

The treatment of chronic pancreatitis is that of the disease of the biliary tract found at operation. J. B. Deaver (Boston Med. and Surg. Jour., Feb. 8, 1917).

In a series of 18 cases of acute pancreatitis, gall-stones were found in 15. In 11 cases the gall-bladder was drained (with 3 deaths) and in 2 the gall-bladder and one common bile-duct were drained, both patients recovering. In 4, the operation was limited to the pancreas; 3 of these patients recovered and 1 died.

Too large an incision in the pancreas presents the risk of hemorrhage difficult to control. Scarification of the peritoneum over it should be sufficient to permit the contact of gauze drainage with the surface. A few blunt punctures of the pancreas may be of value in opening up the ducts and providing an outlet for secretion. Drainage should be instituted by means of gauze and tubes. J. B. Deaver (Surg. Clin. No. Amer., i, 1, 1921).

Cancer.—A radical operation for cancer of the pancreas is hardly to be considered, and the only palliative procedure recognized is done for the relief of obstruction of the intestine or bile-tract.

Cysts.—As a rule these can only be dealt with by incision and drainage. In a few cases small encysted collections of fluid affecting only a portion of the organ have been excised outright. In a few other cases cysts have first been opened and drained and then excised as a subsequent stage of procedure.

Case of a woman presenting a very tender and immovable tumor in the lower epigastric and upper umbilical regions. Operation revealed the stomach, gastrocolic omentum and transverse colon flattened out over the mass and adherent to it. The tissues were all edematous. An approach was made through the mesocolon and the cyst tapped, yielding 4 quarts of viscid fluid. With the exception of the head, the entire pancreas was lying in the cyst; it was gelatinous in appearance. Two chromic catgut sutures were slipped around it, one at the tail, the other at the neck, and about three-fourths of it removed. The drainage tube continued to drain for 43 days. The patient left the hospital on the fortieth day, practically well. J. T. Mason (N. W. Med., xvii, 24, 1918).

Calculi.—When, as occasionally happens, the pancreatic duct is obstructed by a calculus the condition cannot be diagnosticated readily, but is recognized when operating for some other condition, usually for gall-stones. A pancreatic calculus may sometimes be distinguished from a gall-stone with the fluoroscope. The indication is then the same as in obstruction of the common duct.

One of the few surgeons who have

discussed typical pancreatic opera-
tions is Villan, but it is not easy to
determine what, if any, portion of the
work he describes has been done on
the living human being. For those
interested we append a synopsis of
his work.

The term **pancreatotomy** is applied
to incision of any portion of the organ
or its surrounding tissues, for any
purpose. If followed by suture it is
termed pancreatorrhaphy. Pancrea-
tostomy or fistulation of the pancreas
is simply pancreatotomy with drain-
age, and is a frequent procedure in
the surgical treatment of cysts,
abscesses, etc. Pancreatectomy, par-
tial or total excision, is used chiefly
in tumors of the organ (and in trau-
matisms and connection). These
operations will be considered else-
where in detail. Pancreaticotomy,
pancreaticostomy, and pancreatic an-
astomoses will also be considered in
detail.

Pancreatectomy.—This is neces-
sarily partial. It has been done only
to the extent of excising tumors. The
tumor must first be freed from any
attachment to neighboring organs as
well as from the pancreas itself. The
excision of the tail of the pancreas is
attended with much less danger. The
tumors here are more likely to be
pedunculated. Median laparotomy is
followed by liberation of the tumor,
traction and application of strong
forceps or ligatures, which prevent
the entry of blood and pancreatic
juice into the peritoneal cavity. The
pedicle is then divided and cut and
sutured, peritoneum sutured, and
wound closed. It is often prudent to
tampon and drain. Excision of the
head of the pancreas is difficult and
dangerous. Either a part or the

whole may require removal. The
tumor is detached with scissors and
bleeding vessels ligated. The ducts
of Wirsung and Santorini should be
left intact, although the preservation
of either one will suffice.

If Wirsung's duct should be
divided it is usually sutured, and the
same is true of the common bile-duct
should it be injured, although at-
mospheric pressure will sometimes
serve to restore continuity of wound
margins well enough. The operation
is finished by suturing the remains of
the pancreas to the duodenum.

If the entire head of the pancreas
is to be extirpated, it is necessary
first to ligate the pancreatic duodenal
artery and the right gastroepiploic.
The duodenum must not be separated
from the superior mesenteric artery.
Wirsung's duct and the common duct
must be kept intact when possible;
otherwise they must be preserved by
anastomosis.

The entire pancreas can hardly be
excised as a routine procedure, al-
though the operation may be suc-
cessfully performed on animals and
even on man. It is followed by diabetes
mellitus.

Pancreaticotomy.—This operation
consists in incising the pancreatic
duct for calculi. The duct, as in
the corresponding operation on the
common bile-duct, may be approached
directly or indirectly through the
duodenum.

Simple Pancreaticotomy.—After lap-
arotomy and exploration, if a cal-
culus is found therein, the canal is
incised, and the concrements removed
by forceps or other apparatus de-
signed for the purpose. Suturing of
the cut duct is not necessary. A
fistula naturally remains (pancreati-

costomy), but has a tendency to close spontaneously.

Transduodenal Pancreaticotomy.— The duodenum is lifted upward. Incision should be made in the anterior portion, and while some surgeons advocate a transverse, others prefer a horizontal incision. The ampulla of Vater should now be located, and if a pancreatic stone is present the opening may be incised in order to extract it. Suture of the incision is not necessary.

Cathetering of the pancreatic duct and crushing of large calculi are recent procedures in connection with this operation.

Pancreaticostomy and pancreatico-enterostomy have been done very extensively in animal experiment. In human surgery, incision of the pancreatic duct with drainage has been practised, but the operation of pancreaticoenterostomy, which conserves the pancreatic juice in the intestine, is much more rational, and in several instances anastomoses have been effected between the canal of Wirsung and some part of the digestive tract.

The pancreaticoduodenal region is exposed as for pancreaticotomy. Sutures or Murphy's button may be used. The dilated duct should be freed from adhesions and either grafted into the intestine or, what is preferable, a lateral anastomosis may be made. Pancreatic fluid coming in contact with the other tissues may cause local or distant necroses.

SURGICAL AFFECTIONS OF THE SPLEEN.—Abscess.—Splenic and perisplenic abscess will in all likelihood end fatally unless some unusual path is taken by the burrowing pus. Incision and drainage is the usual procedure, but, if the spleen is freely movable or readily freed from adhesions, splenectomy may be the indication of choice.

Cysts.—Simple and parasitic cysts of the spleen are best treated by incision and drainage in the same way as we treat abscesses. If the spleen is not bound down by adhesions, the operation may be done more safely as a two-stage procedure, the first of which consists in suturing the cyst wall to the abdominal parietes without opening of the former, and waiting for forty-eight hours for the formation of protecting adhesions.

Splenomegaly.—Enlarged spleen from whatever cause is usually left to medical resources, unless it becomes so large as to cause serious pressure symptoms, in which case removal of the spleen may become a necessity.

Floating Spleen.—While splenopexy has been sometimes done for this condition, most operators prefer the more radical removal of the spleen because of the difficulty of holding this organ with sutures, due to its friable tissues. The spleen may be fixed through an incision made obliquely along the left costal margin to the quadratus lumborum muscle. The patient is placed in the abdominal position upon a pad or air cushion similar to that used for forcing the kidneys against the abdominal wall. The peritoneal surface of the spleen is scarified, and so is the corresponding peritoneum of the abdominal wall. Kangaroo-tendon interrupted sutures entered at the lowest margin of the spleen serve to fasten it nearly in normal position, and a packing of gauze with a protecting apron of gutta-percha tissue gives support until supporting adhesions have formed.

Rydygier, for fixing the spleen, makes an incision in the middle line of the abdomen high up, and forms a pocket in the parietal peritoneum through a transverse peritoneal incision, and then with the fingers forms a pouch, into which the lower half of the spleen fits. The spleen is secured in this pouch by a few points of suture.

Neoplasms.—Solid tumors of all kinds and tuberculosis require early removal of the spleen.

TYPICAL OPERATION OF THE SPLEEN.—Splenectomy.—The typical external incision is median in traumatic cases (not considered here), but in all others either the semilunar line or one following the costal arch at a distance of an inch or so gives better access to the pedicle. The next stage is purely exploratory and involves division of peritoneum and examination for adhesions. If there are no diaphragmatic or pancreatic adhesions, it is usually possible to isolate the organ, although extensive ligation may be required. It is sometimes necessary to free the spleen from the pancreas by sacrificing a portion of the latter. The organ is then lifted out of the wound, and packed about with gauze. It must be remembered that the spleen is very easily wounded before it can be ligated off, and that profuse parenchymatous oozing will then delay the operation. As in other operations on abdominal viscera, traction on the pedicle may induce shock, because of the intimate connection with the solar plexus.

The next stage consists in ligating the spleen vessels, which is accomplished by tying off the splenorenal ligaments and gastrosplenic omentum and ligation of the vessels of the

hilum. The latter is naturally the ideal choice, but the delay involved adds to the dangers of shock, and unless the patient is in sound condition to withstand operation it may be advisable to transfix the pedicle in one or two planes according to its width, and ligate each by itself. It is well to have apparatus ready for intravenous infusion, which may be begun at any moment that danger from hemorrhage appears.

The after-treatment calls for no special principles. When the danger from hemorrhage or sepsis appears to be slight, the external wound may be closed at once.

In malaria and leukemia the results of splenectomy have been discouraging. In polycythemia, Banti's disease, and hemolytic jaundice, however, they are more promising. T. Rovsing (Hospitalstidende, Feb. 21, 1917).

After splenectomy in 2 patients, the author found a tremendous bone marrow stimulation immediately after operation, as evidenced by marked leucocytosis, increased nuclear red forms, and increase in the large mononuclears and transitionals. One year later the differential count was much the same, except for the increase in the lymphocytes and marked increase in the nucleated red cells. There must be a more essential factor in the blood cell destruction than the spleen. The spleen seems to have a very definite relation to bone marrow cell production, and has a most definite relation to the maturing of the red cells, especially in the destructive metabolism of their nuclei. In the 2 patients, who returned after a definite remission, there was much greater evidence of hemolysis than before. Gilbert (Mich. State Med. Soc. Jour., Sept., 1917).

In diseases of the spleen it is absolutely essential that the surgeon should realize that physical findings are of minor importance, and that a

correct diagnosis must depend on the clinician who in turn must in large part rely on the various laboratory findings and special diagnostic methods. The surgeon adds his opinion as to the advisability of splenectomy, based on the condition of the patient and the probable benefits from the operation.

The essential features in the operation as performed in the Mayo Clinic are as follows: The accessory adhesions and gastrosplenic omentum are separated, divided, and ligated. The dislocation of the spleen can usually be accomplished by stripping the adhesions with the fingers. In a few cases it is necessary to divide adhesions between clamps. After the spleen has been displaced a large pack may be introduced into the space formerly occupied by it. This pack serves to support the organ, and if well placed and left undisturbed, will often obviate difficult ligations of veins of some size. The spleen is now carefully elevated, and tracted toward the midline. Unless accessory vessels are encountered along the posterior border of the pancreas, the pedicle is ligated. A very exact and safe method is first to carefully expose and individualize the arterial and venous branches in the pedicle from the posterior aspect by dividing the fibrous investment of the pedicle. The successive division of each arterial and venous trunk beginning with the lateral vein on each side of the fan-shaped pedicle will permit a very useful mobilization of the spleen, so that the clamping of the central portion of the pedicle which usually contains the splenic artery or its largest branch, is very much favored. Usually torn veins can be ligated, but it may be necessary to leave the gauze pack in place for a few days.

The difficulties of splenectomy depend to some extent on the condition present. In pernicious anemia it is practically never attended by technical difficulty. In hemolytic jaundice, it is usually without special risk, though the spleen is occasionally very large. Splenic anemia is most often associated with high operative risk, particularly in advanced stages, because of thrombotic changes in the splenic and accessory veins. The same is true in hepatic cirrhosis. In the less common diseases splenectomy has no special risks. In the cirrhotic and ascitic stage of splenic anemia, convalescence is protracted and uncertain. D. C. Balfour (Inter. Abst. of Surg., Jan., 1918).

Splenectomy may be very difficult when the spleen is fixed to neighboring organs by old, firm adhesions. Section of such adhesions occasionally results in fatal hemorrhage or may call for long manipulations producing shock. In such cases the writer decorticates the spleen, the plane of cleavage lying beneath the adhesions and between the thickened capsule and splenic tissue proper. By incising the capsule and inserting the fingers beneath it the spleen can be rapidly decorticated and freed. Previous ligation or compression of the pedicle between clamps allows easy completion of the operation.

A case is reported in which the hypertrophied spleen was removed by this method. The organ was sclerotic and adherent close to the diaphragm and the posterior abdominal wall. P. Lombard (Bull. et mém. Soc. de chir. de Par., xlvii, 826, 1921).

SURGICAL DISEASES OF THE LIVER AND BILIARY PASSAGES.—The chief occasion for surgical intervention in these localities is gall-stone disease and its numerous consequences, for the relief of which typical operations are required. Surgical affections of the liver proper, while numerous, are less frequent, and for the most part are relieved by simple general procedures, as incision and drainage.

Abscess of the Liver.—Here may be considered abscess of the liver proper, and suppurative pericystitis.

As soon as the diagnosis is made the pus should be drawn off with an aspirating apparatus, and most surgeons prefer to make an exploratory incision for this purpose. In some cases it may be necessary to excise one or more ribs and go through the pleura, in which case the operation should consist of two stages in order to allow protective adhesions to form. After the pus has been removed an incision should be made of such character as to insure complete drainage, and the abscess cavity allowed to close. If much liver tissue has to be divided to expose the abscess cavity, it will be necessary to use the cautery for hemostasis.

Subphrenic abscess may be considered here, although it may occur on the left side and have no connection with the liver. The general principles of operation here are the same as in abscess of the liver—exploration, aspiration, and eventually incision and drainage. It may be necessary to go through the thoracic wall.

Cysts of the Liver.—Hydatids should be extirpated if possible, the operation amounting to hepatectomy, which see. So radical a procedure is seldom carried out, and the usual intervention, both for hydatids and nonparasitic cysts, is incision and drainage, with the possibility of going through the thoracic wall. The operation may be done in two stages with an interval for the formation of adhesions, or it may be done in a single sitting, the cyst being sutured to the operation wound before incision.

In echinococcus disease of the liver, pain does not form part of the clinical picture, but there may be an inflammatory reaction with adhesions which bring pain, and may even simulate gall-stones. The pain is a warning of infection. In one man of 38 years, a catarrhal jaundice and apparent gall-stone colics compelled an operation, but no gall-stones could be found. The common bile duct was enlarged but was not opened. At a later operation, it was found full of hydatid cysts and a large cyst found in the liver was evacuated. In the differentiation from gall-stones, the shape of the enlarged liver, especially its anterior outline, is important. If the organ is not enlarged, differentiation may be difficult. A. Chauffard (Annales de Méd., Paris, Nov.-Dec., 1917).

Neoplasms.—A single focus of primary cancer may sometimes be removed by hepatectomy; sarcoma is inoperable.

Cirrhosis.—This has been considered under Ascites (Surgery of Peritoneum).

Hepatoptosis.—Hepatopexy is done usually in conjunction with other operations. The liver is scarified or brushed on the cephalad surface, and one of several methods in addition for retaining it *in situ* are essayed. The author includes shortening of the suspensory ligament.

Cholelithiasis.—Simple accumulation of gall-stones, apart from the complication and secondary mischief, demands surgical removal. The choice then lies between cholecystostomy and cholecystectomy.

Peterson found gall-stones in 135 out of 1066 laparotomies for pelvic disease. Kelly found them in 14.5 per cent. and in the Mayo Clinic they were present in 17.1 per cent. of uterine myomata. The reasons for this large percentage of gall-stones in pelvic diseases are: (a) the high average age; (b) the high percentage of patients who have borne children; (c) the proportion of uterine and ovarian neoplasms present. He advocates a routine examination for

gall-stones unless there is some contra-indication. When stones are removed, from 85 to 90 per cent of the patients will have no further trouble; otherwise 30 per cent. will suffer from further gall-bladder symptoms. His conclusion is to remove the gall-stones at the first operation when it can be done with safety. J. M. Neff (Intern. Abst. of Surg., Jan., 1919).

Cholecystitis.—When the gall-bladder has become chronically inflamed, altered by disease and adhesions, it should be extirpated. Partial cholecystectomy is not looked upon with favor. If the process is relatively mild, with the ducts free and intact, cholecystostomy may suffice, but, like the appendix, a gall-bladder once infected is always infected.

Obliteration of Bile-passages from Without.—This is most commonly due to cancer, but may be due to other tumors and inflammatory processes. The typical operation for obstruction from without is an anastomosis between gall-bladder and intestine (cholecystenterostomy). When this is contraindicated permanent drainage by a biliary fistula (cholecystostomy) is the only resort.

TYPICAL OPERATIONS ON BILIARY PASSAGES AND LIVER.—These are few in number, viz., cystostomy, cystectomy, and choledochotomy, cholecystenterostomy, excision of liver. Other operative procedures appear to necessitate only general principles, such as exploratory laparotomy, evacuation of pus, etc. The typical operations on the biliary passages are performed for cholelithiasis, incidentally including chronic cholecystitis.

In gall-bladder operations the writer incises the posterior sheath parallel with the tendinous fibers of the transversalis, *i.e.*, nearly transversely. The level of incision is about an inch above the free end of the gall-bladder, a small opening being first made for confirmation of the diagnosis with the finger. The incision can then be enlarged to the middle line and laterally. The transversalis (posterior sheath) can, with the gloved fingers, be separated from the internal oblique with ease. After the gall-bladder procedures the cut edges of the transversalis can be whipped together with catgut sutures under absolutely no tension. The support given by the uncut transversalis renders tension stitches unnecessary and facilitates closure of the anterior sheath and skin. McArthur (Surg., Gynec. and Obstet., Jan., 1915).

Dangers of delay in operating in gall-bladder cases emphasized. The condition may be divded into 3 stages: (1) That of cholecystitis, occupying the 5 or 10 years preceding the operation, and which has hitherto been looked on with entirely too much indifference and complacence; (2) that in which stones are present but cause no complications in the ducts; (3) that of the terminal condition, *e.g.*, empyema of the gall-bladder, gangrene, pancreatitis, etc. In the first stage the treatment indicated is cholecystectomy, which is followed by practically no recurrences or secondary operations. The second stage cases should also be treated for the most part by cholecystectomy. In the first stage the operative mortality is less than 1 per cent., and in the second, 3 to 5 per cent. No cholecystostomies should be done in the first two stages, except in emergency cases, where the patient is in a bad condition at the time. In the older, third stage patients seen 20 or 30 years from the beginning of their trouble, drainage of bile is likewise ineffectual, and cholecystostomy often does not result in the removal of residual stones. W. Wayne Babcock (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 30, 1917).

Among 800 gall-bladder and other biliary cases coming under the writer's observation since January, 1916, 8.5 per cent. (70 cases) were secondary (there were also a few tertiary) operations. Of the recent series, 51 patients were originally operated by other surgeons, the remaining 19 having been operated on by the writer. In 36 of the 51, recurrence took place after a cholecystostomy, and in 15 after cholecystectomy. The longest interval between operations was 15 years. The average interval between operations in this group was about 5 years and 9 months, the average period of freedom from symptoms being about 2 years and 3 months. In his personal series it was found that in 8 cases the symptoms recurred after primary cholecystostomy, 1 after choledochostomy, and 10 after cholecystectomy, or 1.3 per cent. after removal and 10 per cent. after drainage operation. The great variance between recurrences after radical surgery of the gall-bladder and those after conservative surgery shows that **radical surgical treatment** gives the greater prospect of a permanent cure. J. B. Deaver (Jour. Amer. Med. Assoc., Apr. 17, 1920).

Simple Cystotomy.—The gall-bladder, having been exposed, is incised between two toothed forceps, and the stones if present removed with finger or blunt curet, taking care to remove all possible concrements, some of which may lie close to or in the opening of the cystic duct. One finger should be applied along the bladder externally, to aid in localizing concrements. Folds and diverticula resulting from cholecystitis may contain concrements. The cystic duct and common duct must be palpated and, if stones are contained therein, choledochotomy may be required. The author prefers amputation of the greater part of the gall-bladder as a rule, because it removes an infected

structure and avoids the distress caused by the lower margin of the liver impinging upon a gall-bladder sutured to the abdominal wall.

Cystostomy.—Cystostomy with **Drainage.**—This form of cystostomy is really then a partial cystectomy. The tube remains in position eight or ten days, the bile escaping freely. After the tube has been withdrawn, a little bile may escape up to a week or so longer. As a rule, these fistulæ close spontaneously without trouble.

Cholecystostomy now shows a higher mortality rate than a few years ago. This is because it is now done in extreme cases of severe gall-bladder infection with complications.

Reoperations in gall-bladder disease are necessitated by recurrence of stones or by the formation of adhesions or fistulæ. Stones are much more common after cholecystostomy, but may be formed in the ducts after cholecystectomy. Adhesions of such a character as to necessitate reoperation because of pain or interference with the mobility of the stomach or intestines are formed usually in severe cases in which there is suppurative peritonitis and long-continued drainage is necessary. In a given case, adhesions should not be more frequent or severe after removal of the gall-bladder than after drainage, provided the removal is done carefully.

Fistulæ necessitating reoperation open from the gall-bladder or ducts into the small intestine, the colon, or the stomach. When the adhesions are very dense and extensive, gastro-enterostomy gives the best permanent relief. J. H. Branham (Amer. Jour. Obstet. and Gynec., i, 331, 1921).

Cystectomy.—Surgeons have proved by experience that cystostomy had many drawbacks. It is the conservative method, but leaves behind a diseased gall-bladder, which invites new surgical disorders. Adhesions which are invariably present cause

the organ to lose its mobility, thus increasing the liability to further infection. Cystectomy, an operation originally performed only on suspicion of cancer, has been the choice of the author for many years, the suggestion having come from Langenbeck's discovery of the safety of extirpation of the organ originally, and this idea confirmed by many operators later.

Excepting in cases of cancer the author prefers the same operation for cystectomy that he does for cystostomy, for the reason that the small portion of gall-bladder which is allowed to remain allows of easier fastening to the drainage tube, and lessens the annoyance of hemorrhage from the artery and vein of the cystic duct.

Cholecystectomy should be the predominant operative procedure in biliary surgery. With the destruction of the lining mucosa of the gall-bladder by violent disease, the necessity for cholecystectomy is less evident, while the mortality of the operation for violent infection in the debilitated is such that a safer operation should be substituted; therefore *drain for gangrene, extirpate for catarrh*. Choledocho-duodenostomy is indicated in elderly debilitated patients who have or have had jaundice, or the evidence of common duct obstruction; who will not well bear a dochotomy, who may have overlooked or residual stones, or who have duct obstruction, as in inoperable carcinoma or in certain cases of mucocele, not to be treated by cholecystectomy. It is also to be considered in the treatment of Hanot's cirrhosis of the liver. The patients least able to withstand the shock of operation are those who have had prolonged external drainage of bile, jaundice, or acute septic choledochitis. The operative treatment should, if possible, antedate and pre-

vent these complications. Excluding technical operative errors the mortality of biliary surgery comes largely from delayed and secondary operations. W. Wayne Babcock (Can. Pract. and Rev., Aug., 1917).

Gall-stone colic may be a persistent symptom even where no gall-stones can be found. Cholelithiasis should be operated upon as soon as the diagnosis is made. A diseased appendix, if allowed to remain, will continue to distribute infection to the gall-bladder after simple drainage of the latter.

As regards the relative indications for cholecystectomy and cholecystotomy, the author believes that the former should be performed under the following conditions: (1) Stones in the gall-bladder; (2) cholecystitis without stones; (3) gall-bladder wall disease; (4) stones or other obstructions in the cystic duct; (5) adhesions around the gall-bladder which interfere with its pumplike action; (6) the strawberry or papillomatous gall-bladder; (7) malignancy. Cholecystotomy should be used: (1) In pancreatitis with jaundice; (2) in the very old and feeble cases or with poor physical condition; (3) where the operation would be dangerous because of inaccessibility of the gall-bladder. The appendix should be removed whenever there is the least suspicion that it is diseased. F. R. Benham (Annals of Surg., Oct., 1917).

Technique.—The gall-bladder, having been exposed, is freed from adhesions and from the normal peritoneal reflection to the surface of the liver. The presence or absence of gall-stones in the bladder is only of incidental importance, because it is for infection of the gall-bladder that the operation is done. The freed gall-bladder can be handled very much as one would handle the appendix, and the operation from this stage on is somewhat similar. Any bile or concretions which are found in the lower

part of the gall-bladder or the cystic duct are stripped out with the fingers into the cavity of the gall-bladder proper, which remains unopened. The part which has been emptied by stripping with the fingers is then ligated or clamped with a pair of forceps to prevent the return of contents to the region of the operation. A longitudinal incision large enough to allow the entrance of a small soft-rubber catheter is then made below the clamp or ligature, and extending as far as or into the lumen of the cystic duct. The catheter is introduced into this opening and tied in place with a catgut suture piercing the wall of the cystic duct and catheter alike. This avoids displacement caused by vomiting. The next step consists in tying another catgut suture snugly around the cystic duct or the lower portion of the gall-bladder so firmly as to cut off all circulation in the walls. The gall-bladder is then amputated between the clamp and ligature, and the lumen of the stump at the point of compression by the ligature may be sterilized like the stump of the appendix, by brushing it with 95 per cent. carbolic acid neutralized a moment later with alcohol. The catheter, acting as a drainage tube, is then left escaping from any convenient angle of the wound of the abdominal wall. In two or three days the constricting suture is usually absorbed and the flow of bile then begins through the tube, which can be removed at any time subsequently, because the suture of catgut fastening the catheter to the cystic duct is absorbed at the same time with the constricting suture. The advantage of this technique is that peritoneal adhesions

have had time to wall in the area of operation so that bile or septic fluid escaping from the region of the stump makes its way safely to the surface. Sometimes it is an advantage to split the catheter longitudinally throughout its entire length, and to lay a strand of gauze loosely in the catheter because this gives us capillary attraction to help in guiding bile or septic fluid to the surface; and if the walls of the catheter are prevented from closing entirely, any blood or other fluid between the stump and the external incision is drawn out the same way by capillarity.

Some surgeons do not consider partial excision as a typical operation. They state that cases occur in which the gall-bladder is so fragile that its liberation would be impossible, but such cases make a small part of the ones actually dealt with in practice, and. practically the same principles can be observed.

Cholecystectomy without drainage advised in simple gall-bladder infection, as contact of the bile with the peritoneum readily induces adhesions. The writer uses a right rectus incision, curving toward the xiphoid at the upper end. An incision is made into the hepatoduodenal ligament, and the pelvis of the gall-bladder grasped and pulled upward while a right angle clamp seizes the cystic duct and artery. A ligature is now placed around the cystic duct close up to its junction with the common duct, a second ligature is placed around the cystic duct and artery and the two are cut, the gall-bladder being dissected out from below upward. The stump of the cystic duct is secured in the ligament by means of a crown suture passing through both layers of peritoneum and around the stump. The raw surface is covered with peritoneum and the abdomen closed without drainage.

Among 549 operations there were 398 cholecystostomies with a mortality of 1.7 per cent., 107 cholecystectomies, 0.9 per cent., and 44 choledochotomies, 9.0 per cent. There were 26 secondary operations, 21 following cholecystostomy and 5 choledochotomy. A. M. Willis (Jour. Amer. Med. Assoc., Dec. 8, 1917).

Of 2027 biliary operations in 2 years at the Mayo Clinic, 219 (10.8 per cent.) were secondary. Of these, 120 were for the removal of gall-bladders which had been drained previously. There was only an 0.8 per cent. mortality, showing that the risk in the secondary operation is no greater than in the primary. In 109 of the 219 operations, calculi were found either in the gall-bladder, the ducts, or in both; 153 patients had cholecystitis. Adhesions were especially noted in 148 cases, and in 41 there was a definite pancreatitis. Either a mucous or a biliary fistula was present in 37 cases. Seventeen of the 209 patients were definitely jaundiced. In 64 of the 219 cases both the primary and secondary operations had been performed in the Mayo Clinic. In 12 of these, the primary operation was cholecystectomy. Judd and Harrington (Annals of Surg., Apr., 1918).

In cholecystectomy, if adequate dependent drainage is not established through a counterincision at the bottom of Morrison's pouch, then it must be ample through the abdominal incision, so that by no chance will there be an accumulation of fluid at any one point which may be dispersed by the respiratory movements. If the mucous membrane of the gall-bladder is gangrenous; if there is chronic infection of the gall-bladder; if there is a stone embedded in the cystic duct; if the wall of the cystic duct is thickened; or if the wall of the gall-bladder is thickened by scar tissue as a reaction to infection—then mere drainage of the gall-bladder will very frequently be followed by recurrent obstruction and infection, and in these cases cholecystectomy is rec-

ommended. On the other hand, if the gall-bladder has approximately normal walls, and if the cystic duct is approximately normal, then no matter what the size or the number of stones, if the operation is performed with due care there will be rarely if ever a postoperative pathologic cycle. In cholecystectomy the gall-bladder should be exposed by an ample incision so that there is free access to the base of the gall-bladder; the freeing of tissue should be made by sharp dissection, care being taken not to injure the liver even slightly.

The entire gall-bladder should be freed from its attachment so that ample opportunity may be given for determining the exact place at which the gall-bladder ends and the cystic duct begins, the division being made just proximal to this point.

In death from "liver shock" following operation, the common causes are ether anesthesia, suboxidation from deep and prolonged anesthesia, trauma, and low blood-pressure. The use of a **local anesthetic** coupled with **light gas** and **oxygen anesthesia;** minimum trauma, secured by an ample incision, by sharp knife dissection, and by as brief an operation as is consistent with good surgery; **blood transfusion** if the blood-pressure is low, and **morphine** in case of pain, obviate or minimize these causes. In addition, the activity of the liver cells is increased by the application of **local heat** and by **abundant water.** To this end large **hot packs** should be used and adequate water equilibrium established before and after operation. Crile (N. Y. State Jour. of Med., Oct., 1920).

Choledochotomy.—This operation comes into play when after cystectomy the common duct or the hepatic duct is found diseased or containing concrements. A wide external incision is requisite when it is believed that this operation is indicated. Exposure may be difficult on account of the conformation of the thorax, or

when adiposity interferes. It may be necessary in such cases for an assistant to draw aside all the surrounding viscera widely with the hands, with gauze beneath the fingers. If adhesions are absent the common duct may be lifted into the field with the fingers or a pair of padded forceps. The peritoneal covering is slit. The large vessels—hepatic artery and portal vein—behind the biliary passages are to be avoided. A small vessel running obliquely across these must be held aside or tied and divided. Two lymph-glands in this locality may be so enlarged and inflamed as to simulate concrements. The common duct must now be examined for concrements and inflammation. If concrements are palpable, the duct is opened between slipnooses or forceps. Bile will at once escape and must be caught up with gauze pledgets and the stones, if present, removed with small forceps or curets.

As a rule, however, extensive adhesions are present, and the operation is much more complicated. These adhesions must be separated as far as possible, and if the cystic duct has not already been opened it should be incised. If the object were not primarily to extirpate the gall-bladder, this should now be done and the cystic duct divided. The chole-dochus should next be sounded through the opening, the finger palpating the outside of the canal. If concrements are present, the cystic duct may be laid open slowly until the common duct is reached. By the aid of small curets and forceps, and palpation externally, small concrements may be extracted. If necessary the incision may be continued into the common duct as far as the duodenum. Extraction of stones from an inflamed or dilated chole-dochus requires the same precautions as in the case of the gall-bladder. That portion of the duct behind the duodenum is very difficult of access, unless the reflection of peritoneum from the duodenum is first cut away. In cases of this sort it has been necessary to enter the duodenum.

The conservative method is to draw the duodenum to one side after freeing the peritoneum, but this is believed by some to affect the nutrition of the latter unfavorably. A drainage tube is inserted into the choledochus, and the latter sutured up to the tube by most operators, but the author usually dispenses with sutures, excepting the single one for holding the tube in place, because the walls of the duct normally fall together well, and atmospheric pressure keeps the cut margins together as well as sutures would do it, unless much unusual injury has been caused by the operative work.

Writing on drainage of the common duct after cholecystectomy, the author considers that such drainage by way of the stump of the cystic duct is only a temporary procedure. When prolonged drainage of the common duct is needed, he opens the common duct and introduces a T-shaped rubber drainage tube. He has a number of patients wearing these tubes. This form of drainage is introduced in certain cases of pancreatic lymphangitis, and chronic interstitial and interacinar pancreatitis. Early drainage of the common duct by this method or by a cholecysto-duodenostomy is the only chance for the cure of pancreatic diabetes. Deaver (Annals of Surg., Apr., 1916).

In operations on the biliary passages the common duct should be

opened: (1) When there are many small stones in the gall-bladder or the cystic duct; (2) when the common duct is enlarged and its walls greatly thickened; (3) when chills, fever, and jaundice have been present before the operation. Eisendrath (Jour. Kans. Med. Soc., June, 1917).

In some cases of new growth or injury, the damage to the hepatic duct may be such as to necessitate *hepatico-duodenostomy*. A slightly curved flap is dissected out of the duodenal wall, leaving an opening into the duodenum about 2 cm. in diameter. The flap is then approximated to the posterior and lateral aspects of the stump of the hepatic duct so as to permit muco-mucous union of the posterior half of the circumference of the duct. The remaining free margins of the opening are sutured to the liver capsule just above the end of the hepatic duct by continuous catgut sutures so that the opening in the duodenum not occupied by the end of the hepatic duct is effectually closed. D. C. Balfour (Annals of Surg., Mar., 1921).

Cholecystenterostomy.—A typical operation indicated is closure of the biliary passages from without. A long abdominal incision is required, oblique or angular, beginning at the ensiform cartilage and carried down through the right rectus muscle. The intestines are controlled by gauze. If gall-stones are present they are removed, and it must also be determined that suspected cancer of the pancreas is not a calculus in the pancreatic region. A choice of intestinal locality for anastomosis is then in order.

The duodenum is the ideal region, but in practice a high jejunal anastomosis is often preferable. The gallbladder is emptied upon gauze, and the apex seized with a clamp. A loop of jejunum is similarly held with the fingers. Both structures are opened

to the extent of a finger-tip, as in gastroenterostomy, and the suture is also performed as in the latter. This locality may be fortified with omentum, if the operator wishes.

The Murphy button is useful for this anastomosis and is used by many operators, but simple suture suffices for most cases.

One must be quite sure that the cystic duct is competent before attempting cholecystenterostomy. The gall-bladder should not be too seriously pathologic. Anastomosis with the colon is dangerous. Anastomosis with the duodenum above the ampulla of Vater, though more difficult than with the jejunum by the retocolic method, is ideal physiologically and is the method of choice in non-malignant conditions where a permanent stoma is considered, *i.e.*, in obstruction of the duct not removable by choledochotomy or stenosing injuries following choledochotomy. Anastomosis by the retrocolic method with the jejunum should be adopted wherever anastomosis with the duodenum is impossible through adhesions or other causes, and is the method of election in all malignant conditions. By either method it is essential to establish a liberal stoma. All added anastomoses are of doubtful utility. As in cholecystostomy or cholecystectomy, drainage of Morison's pouch is essential, with the added precaution of not allowing the drain to come in contact with the suture line. H. A. Shaw (Intern. Jour. of Surg., Aug. and Sept., 1916).

Excision of Liver; Hepatectomy.—Indicated in tumors chiefly, including cysts, and sometimes after traumatisms. When a pedicle is present or the mass occupies the margin of the liver, hepatectomy is very easily performed by the aid of ligation.

According to Garré, extensive resections of the liver can be carried out with the

most simple means. If care is taken not to stretch the vessels in cutting through the organ and not to pull them out, it is not difficult to apply hemostatic forceps and a ligature. The vessels cut obliquely have to be taken care of by circular suture. Compression suture of the wound in the liver and catgut suture of the surface are the safest means of hemostasis. It is best to press together two wounded surfaces of the liver by suture, and, whenever possible, to make a wedge-shaped resection placed in an approximately vertical direction in relation to the margin of the organ. Editors.

When this is impossible the mass is removed step by step, followed by ligation of all bleeding vessels. It is often possible to ligate these in advance of division with a needle armed with catgut. After extirpation it is in order to ligate all lumina of blood-vessels with the aid of a needle rather than with forceps, and then suture the liver with catgut. Buried sutures are undesirable for the liver, however, as blood and bile seep into them. Pressure may be brought to bear for controlling hemorrhage that is not from spouting vessels, in some cases. Pressure is obtained by carrying a long catgut ligature deeply through the wound in the liver, and fastening each end of catgut to a broad plate of sheet lead. If the entering end of catgut is first fastened to its respective plate of lead, the emerging end of catgut can be tightened to any desirable extent before fastening it to the second lead plate. Ears fashioned on the lead plates can be bent over to hold the catgut ends, and silk strands fastened to the plates and led out of the wound serve for removing the plates eventually when the catgut is absorbed. More than one pair of plates may be used for an extensive liver wound.

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ABDOMINAL INJURIES.—

Under this heading will be considered the broad field of injuries of external origin to which the abdomen and the abdominal viscera are liable. These include *contusions,* which are important mainly because of the lesions to which the intra-abdominal organs are exposed; *non-penetrating wounds,* in which the abdominal walls alone are injured, and *penetrating wounds,* in which the walls and the abdominal viscera are penetrated.

CONTUSION OF THE ABDOMEN.—SYMPTOMS.—Whether caused by blows, kicks, spent bullets, the passage of heavy bodies—such as vehicles—over the abdomen, etc., the symptoms attending a contusion in this region are not always such as to call attention to the seriousness of the lesion present. The gravest abdominal injuries may coexist with practically no external or general indication of mischief, the patient walking a long distance, perhaps, without experiencing anything more than slight local pain where the blow had been received.

Although the abdominal walls may be but slightly injured, the lesions may consist of extensive extravasations of blood between the layers, or sufficient laceration of the muscular and other tissues to give rise to more or less local sloughing. Such lesions of the abdominal wall, however, are not always accompanied by injury of the abdominal organs.

Usually, in these cases, according to Scudder, the greater the force the greater the injury, but a trivial blow may result in serious damage to intra-abdominal viscera. A hollow organ, if distended, is more vulnerable than if empty. Inquiry should be made as

to the last mealtime and as to the last micturition. The exact direction of the blow is important. The clothes of the patient sometimes offer some indication as to the injury.

A trifling superficial injury of the abdominal wall may be associated with serious internal lesions, owing to the resistance offered by the abdominal walls and the fragility of the abdominal organs. The external appearances, therefore, should not be taken as a criterion.

From observations of some twenty cases of visceral injury, following contusion of the abdomen, verified by operation or autopsy by Brewer, the most prominent were pain, tenderness and muscular rigidity, and likewise the most reliable. The deep-seated, localized pain following injury, especially increased by pressure, and accompanying local or general muscular rigidity, is one of the most constant signs of intra-abdominal injury. Brewer holds that the association of these three symptoms is almost pathognomonic of abdominal irritation. Pain, however, is often present, with tenderness, in injuries limited to the abdominal wall; but in these instances muscular rigidity is generally absent. In the absence of subcutaneous pain localized tenderness with rigidity is strongly suggestive of visceral injury. Of the three symptoms, muscular rigidity is the most reliable, and sometimes the only sign. In the absence of other diseased conditions spasm of one or more of the abdominal muscles following the traumatism may be looked upon as nature's effort to protect an injured organ from further irritation. Vomiting is a symptom often present,

but not always an accompaniment of severe visceral injury. It is commonly present with involvement of the stomach and upper part of the intestinal tube, and with injuries resulting in severe shock. The signs of free fluid in the abdominal cavity are very suggestive.

In most cases, however, severe contusions of the abdominal wall, whether the deep organs are involved or not, are followed by agonizing pain in the region of the injury, restlessness, nausea or vomiting, marked prostration (indicated by a small, rapid, and irregular pulse), pallor (sometimes attaining lividity), cold sweats, rigidity of the abdominal wall, meteorism, anxiety, and fear of a fatal issue.

All these symptoms bear the imprint of a severe nervous commotion, and, if the extensive distribution of the sympathetic nervous system in the abdominal cavity is borne in mind, the fact will become evident that symptoms usually witnessed immediately after the receipt of the injury are due mainly to the influence of the concussion upon the sympathetic supply. Sudden death has been known to follow a violent blow, especially when received in the region of the solar plexus.

The pain varies according to the location of the traumatism and the sensitiveness of the patient. Very severe at first, it usually becomes less marked after a few hours. It is greatly influenced by shock, profound prostration reducing its intensity by reducing sensation. Great restlessness usually accompanies abdominal pain after injuries, as well as during other diseases, such as appendicitis,

when the suffering is due to a localized trouble. The pain may be radiated in various directions,—the shoulder, the umbilicus, the left axilla, the testicles, etc.—according to the site of the primary lesion. Local tenderness is usually marked over the site of the traumatism.

The vomiting varies greatly in intensity from mere nausea to the most violent expulsive efforts, which are liable, by the strain upon the abdominal organs, to suddenly increase the extent of the lesions. The vomited matter sometimes contains blood, especially if the upper portion of the digestive tract is involved in the injury. Constant and persistent vomiting tends to indicate a contusion accompanied by visceral lesions. According to Berndt, in simple cases the vomiting is repeated but two or three times. When the intestine is ruptured the vomiting is persistent and intractable and liver-dullness is absent.

The degree of shock depends upon the nature and extent of the injury and especially upon the amount of blood lost. When the signs of collapse gradually become more marked, internal hemorrhage from rupture of one or more of the viscera is to be feared.

The pulse, usually rapid and weak at first, gradually becomes stronger and slower if a favorable reaction is about to take place. If, on the contrary, an unfavorable course is being taken and some complication is to occur, its rapidity and tension may become increased. Irregularity is not a favorable indication if it persists. Temperature is independent of the pulse, except when a favorable reaction is taking place, when it may

return to the normal line after having gone beyond or below it. The usual belief that a subnormal temperature always follows internal hemorrhage is fallacious; for it may also be raised. The temperature, therefore, is of no value as a guide.

Hematemesis may assist in establishing the diagnosis of lesion in the stomach or the upper portion of the intestinal tract, while the presence of blood in the stools may do the same as regards lesions of the intestines as a whole, including the colon. But, in itself, this symptom is, by no means, characteristic, since a violent strain may cause sudden engorgement of pharyngeal, gastric, rectal, or hemorrhoidal vessels and then, several days after the accident, blood-rupture ensue. Even when present, streaks in vomited matter or stools are not always indicative of an alarming condition.

Blood in the urine is a more reliable sign of lesion in the urinary tract, especially the kidney and bladder. Anuria is also indicative of lesions in these organs; but, as shock frequently arrests the flow of urine, it is only valuable as a symptom after all symptoms of shock have passed.

Hemorrhage into the orbits and from the ears are occasionally met with when the concussion has been very severe. This symptom does not necessarily indicate that the injury is an unusually dangerous one.

A few hours after the accident the pain usually becomes reduced; the patient may be more quiet and, perhaps, somnolent, although the pulse remains in its former condition. This period lasts between twelve and twenty-four hours. If at the end of this time there be no complication,

a visceral lesion is probably not present. If, on the contrary, the symptoms gradually increase in intensity, the likelihood of grave injury is very great.

In the light of present knowledge, however, the practitioner should not delay active procedures until the patient's life becomes compromised by permitting the mechanical injury produced to start an infectious process, when the manner in which the injury was inflicted and the force applied tend to suggest serious internal lesion. An exploratory incision is sometimes permissible (see colored plate).

DIAGNOSIS.—In abdominal contusions the diagnosis should primarily be based upon the history of the accident, the manner in which the injury occurred, the shape of the body, or bodies, by means of which the traumatism was inflicted, and the degree of percussive force applied, and, secondarily, upon the symptoms present.

The value of abdominal or bimanual vaginal examination of patients while in a hot bath has been emphasized by Carter. In many instances the abdominal relaxation obtained is quite equal to that obtained under an anesthetic, with the added advantage that the patient can help the examiner by voluntary movements, such as deep inspiration, holding the breath, etc.

Report of 2 cases of injury followed by a quiescent period. At operation, the small intestine was found completely severed and the ends of the intestine closed off by the local reflexes so that there was no leakage. After certain injuries to the abdomen there is frequently such a period of from 12 to 24 hours during which the surgeon and patient may decide what is to be done. Purgatives prove harmful. G. E. Armstrong (Jour. Amer. Med. Assoc., Dec. 6, 1919).

Lesions of the Intestinal Tract.— Various theories have been advanced as to the manner in which rupture of the intestine is brought about, but experiments have shown that squeezing of the gut between the compressed abdominal wall and the vertebral column is the main mechanical factor brought into action.

In reporting a personal case of retroperitoneal rupture of the duodenum in which the points of interest were slight general and local reaction from the resulting abscess, due to the relative sterility of the duodenal contents, and also a point of tenderness beneath the twelfth rib, the writer reviews a series of 22 cases. The injury is peculiar to the active working male, and is always due to trauma. In the 22 cases, 82 per cent. were situated in the second or third portions of the duodenum, and 15 showed retroperitoneal extravasations at operation. This is always found either in the root of the transverse mesocolon, in the root of the mesentery of the small bowel, or involving, in addition, the intervening retroperitoneal space, and is usually of rapid formation. The contents is a bloody, bile-stained fluid mixed with gas that soon becomes purulent. The peritoneal cavity is clean or at best contains a very small amount of free blood-stained fluid, probably from a minute injury to some viscus. Peritonitis is undoubtedly delayed for some time by the intact peritoneum, but ultimately occurs. There may appear a fixed tumor in the upper right quadrant, but this was only noted in 2 cases. Of the 22 cases, 20 were operated on and but 3 recovered. No case survived when operation was postponed longer than 24 hours. R. T. Miller (Annals of Surg., lxiv, 550, 1916).

Injury to the bowel by direct violence to the abdominal wall is possible under the following conditions: First, when the force is sufficient to carry the abdominal wall back so

that the bowel is caught between the object producing the force and the body of a lumbar vertebra. The position of the patient at the time of injury with the body inclined forward and a weak, flabby abdominal wall would predispose to this form of injury. A second possible condition in which rupture of the bowel might occur is when it is filled by a solid or semi-solid matter that offers sufficient resistance to rupture the gut before it can recede from the oncoming object producing the sudden blow. A third possible condition is that rupture may occur by reflex stimulation of the intestinal nerves through the nerve supply of the abdominal wall.

Rigidity of the abdominal muscles, pain of a severe type, a strained and anxious countenance, a varying degree of shock, and a rapidly increasing pulse-rate are sufficient signs to lead to a diagnosis and to indicate immediate operation. J. S. Wright (Can. Med. Assoc. Jour., viii, 228, 1918).

Crushing against the ileum is rarely produced. Another, although rare, cause of rupture is the presence, in the intestinal tract, of liquid or semi-liquid material, the sudden circumscribed pressure exerted upon the gut causing it to burst, through overdistention. The small intestine is the seat of lesion in 75 per cent. of the cases of rupture in the course of the intestinal canal. Hence the importance of carefully ascertaining in each case the direction from which the percussive force came, the intensity of that force, and the relative position of the organs between the site of pressure and the spinal column.

Another factor of importance in establishing a diagnosis is the size of the instrument causing the injury. Lesions of the digestive canal, for instance, are usually the result of violent and sudden percussion produced by a body over a limited surface of the abdominal wall.

The predisposing factors are the presence of solid, semisolid, or fluid matter in the hollow viscera; leanness of the individual, and intestinal adhesions.

Any of the above accidental causes of injury being fulfilled, rupture of some portion of the gastrointestinal tract is likely, especially if there is loss of consciousness at the time of the accident, followed by collapse, severe pain, a rapid and weak pulse, vomiting, tympanites due to the escape of intestinal gas into the abdominal cavity, and tenderness and rigidity of the abdominal walls.

Fränkel has laid great stress on the slow rise of the temperature from hour to hour. A pulse above 100, if hemorrhage can be excluded, speaks in favor of rupture of the intestines and incipient peritonitis.

Case of rupture of the jejunum in a boy who was struck in the abdomen while playing football. The main symptoms were vomiting, elevation of temperature to 101° F. (38.3° C.), pulse 118 within a few hours after the accident, some rigidity of the upper abdomen, but marked absence of shock and severe pain. Twenty-eight hours after injury the pulse was 112; the temperature, 100.5° F. (38° C.), the leucocytes, 25,000. Vomiting had occurred 5 times, the last vomitus having a fecal odor. The bowels had acted once; there was slight tympanites. Operation revealed a large rent in jejunum. Suture with drainage of the abdominal cavity was followed by recovery. Leakage from the jejunum is less dangerous than from the ileum, where bacteria are present in greater numbers. F. K. Boland (Jour. Med. Assoc. of Ga., vii, 74, 1917).

Such a diagnosis is further strengthened by hematemesis or bloody stools, the former tending to indicate a lesion of the stomach. Death occurs in 96 per cent. of such cases if unoperated.

In the differential diagnosis of abdominal contusion the greatest feature for an early recognition of the existing conditions is whether there is unilateral or general tension of the abdominal wall, unless there is considerable blood-suffusion at the injured place. Aside from the reflex tension of the abdominal muscles, a slight, but distinct exacerbation of the general condition during the first few hours following the injury is a point of importance. With very careful observation, three or four hours may be allowed to elapse, but even then there is the possibility of error. Koerte reported a case where he was absolutely certain of his diagnosis and had decided to operate; the patient, however, refused operation and made a smooth recovery.

In the *most favorable cases,* where is but a slight tear, the mucous membrane will prolapse and occlude the aperture. Neighboring loops or the omentum will form a layer over the lesion with agglutination or adhesion, so that recovery may take place. If there is exudation of intestinal contents, a circumscribed, encysted abscess may form which is capable of resorption, or secondary perforation into the intestine or outward may occur; but it is equally possible that pus will find the dangerous route into the free abdominal cavity.

In the *most unfavorable cases,* there is neither occlusion nor abscess formation; the inflammation will rapidly spread over large areas or over the entire peritoneum and cannot be checked. As early as four hours, exudate may be found; likewise, fibrinous deposits on the various loops. The more or less fulminating course is not only dependent upon the quantity of the exudate, but also on its infectious nature.

Statistics show the rarity of cases in which the most favorable course, as depicted above, takes place. Of 160 cases of subcutaneous intestinal rupture in which the expectant treatment was instituted, 149 died; of the 11 which recovered, 10 had to be operated during treatment for fecal abscesses and fistulæ. Enderlen (Post-Graduate, July, 1911).

For the detection of intraperitoneal rupture of the intestine from contusion, the abdomen should be carefully examined every hour for pain, intensification of existing pain, and local tenderness. When the indications point to rupture, expectancy should be limited to 1 hour. The writer sutures the rupture or resects the intestine and then mops up the peritoneal cavity without washing it out. He has had 8 complete recoveries and 3 deaths. Soederlund (Nordiskt med. Arkiv, li, No. 5, 1919).

Reports of 30 cases of detachment of the mesentery in abdominal contusion have been found by the writer. In 8 of these the detachment was the only lesion. It usually occurs in the terminal part of the ileum, but in 4 cases it was in the middle part, and in 3 in the first part. The symptoms may be those of internal hemorrhage and acute anemia. Or there may be an acute peritoneal syndrome. In a third type there is a syndrome of simple parietal contusion.

In the first 2 types the symptoms demand **immediate laparotomy.** In the third there is no symptom of internal hemorrhage or peritonitis and the surgeon will probably delay laparotomy. In the author's case absence of symptoms continued for 36 hours. In such cases gangrene of the detached intestine is certain to develop unless a prompt operation is performed. The peritonitis becomes manifest only 24 to 40 hours after the injury. L. Sencert (Bull. et mém. Soc. de chir. de Paris, xlvii, 758, 1921).

Lesions of the Stomach.—Blows seldom cause rupture of the stomach, the elasticity of the organ, even when

containing liquid or semiliquid material, being such as to cause it to escape injury under sudden impact or great pressure. It is also protected by the lower ribs, the liver, and the intestines. Nevertheless, this organ is occasionally involved in traumatism affecting other abdominal viscera. In the majority of cases the rent is found near the pyloric orifice, but the greater curvature may be the seat of the lesion, while the entire organ is occasionally torn from end to end. In the latter case, however, death ensues almost immediately in practically all cases. Pressure during lavage of the stomach may also cause laceration of the mucous membrane.

In the case of incomplete tears there may be hematemesis and severe localized pain resembling that of gastric ulcer,—gnawing and burning in character. This is followed by localized inflammation with tendency to the formation of adhesions. Hemorrhage between the coats of the stomach may also occur in incomplete tears, a cyst-like pocket being formed.

Violent pressure upon the stomach may cause it to be crushed against the spinal column, and the mucous surface be lacerated by interpressure of the anterior and posterior walls of the organ. In such a case a marked lesion necessarily follows, giving rise to copious hematemesis.

Rupture of the stomach implicates the peritoneal coat in the majority of cases, the elasticity of the peritoneal investment being less than that of the two internal coats: muscular and mucous. The contents of the stomach, or a portion of them, escape into the peritoneal cavity and cause severe suffering and shock, followed promptly by death or septic peritonitis. Bryant teaches that a ruptured intestine is probably present, though this is not certain, when, after a diffuse injury to the abdomen or a severe local injury as the immediate result of the accident, there is little collapse, and when vomiting soon becomes a prominent and persistent symptom, with lasting local pain and great thirst, with or without abdominal enlargement.

According to Gluzinski, two signs which enable the physician to diagnose the occurrence of intestinal perforation before peritonitis has had time to manifest itself: 1, distinctness of the murmurs of the heart and respiration during auscultation of the abdomen, due to the presence of intestinal gases in the peritoneal cavity. 2, change in the pulse, which, at the moment of perforation, becomes accelerated, to slacken some hours later, owing to the absorption of putrid gases acting as cardiac poison.

In every case of perforation of the stomach or duodenum, free gas and fluid are present in the peritoneal cavity. The gas may pass between the liver and diaphragm, as shown by the X-ray, and cause obliteration of liver dullness. Much dependence cannot be placed on liver percussion as ordinarily practised, because of the very great variations, both in health and disease. Change of the patient's position, however, will cause the fluid to flow to the dependent part, and the air to rise to the top, thus intensifying the findings. There is tympany over a wide liver area and again flatness over the same area on change of position. Normally there is also a change in the liver percussion note on change of posture, and normal liver changes must be recognized before positive deductions are made. A fair comparison is the difference detected in shifting flank dullness in

moderate ascites and in the normal abdomen. M. T. Field (Boston Med. and Surg. Jour., Feb. 14, 1918).

Lesions of the Liver.—The liver, owing to its friable nature, its size, and its anatomical position, is the organ most frequently injured, because indirect concussion may cause a profound lesion. A fall from a great height into water may thus cause a gaping rent of the capsule and parenchyma and open a large number of vessels. Severe and sudden blows of any kind, especially those involving much surface, over the abdominal wall may thus cause injury to this organ. Again, its softness, which may be increased by hypertrophy, causes it to yield readily to the crushing produced by carriage-wheels, car-bumpers, etc.

Rupture of the liver according to Battle, is an extremely fatal accident, and the symptoms which ensue are usually marked and serious. Shock is present, frequently passing into collapse and death. Short of this there are vomiting, rapid pulse and respiration, pallor, etc. In this accident rigidity of the abdominal wall is very evident, so that it may appear boardlike. Tenderness becomes localized to the hepatic region, and there is shifting dullness in the flanks with the ordinary symptoms of loss of blood, according to the amount of it which is effused; the man becoming restless with a rapid, weak pulse, sighing respiration, and what is called "air hunger." Jaundice may be a late symptom and is therefore of no use in the early diagnosis which is so very important.

The severity of all the general symptoms is usually increased. The pain, when the liver is seriously injured, is peculiar; it radiates from the right hypochondrium to the waist, the scrobiculus cordis, or the scapular region. The respiration is generally embarrassed; there is marked shock.

Examination of the feces may show the absence of bile, especially if the bile-duct is ruptured: an occasional complication. The dissemination of bile in the system causes itching and, after a time, jaundice. The escape of bile into the peritoneal cavity may not give rise to peritonitis, however, this fluid being aseptic. A serous exudate may result from the irritation caused by its presence, forming a composite fluid which may be retained in the peritoneal cavity a considerable time.

The most reliable symptom is the *défense musculaire* emphasized by Hartmann and Trendelenburg. Rigidity is not the proper term for this condition, for rigidity rather denotes a tetanic state of the abdominal muscles, whether stimulated by pressure of the hand or not. It is not marked, except in the gravest cases, shortly after injury, but develops in the following few hours from irritation of the peritoneum by the hemorrhage of intestinal contents from rupture of the intestines. It was especially mentioned twenty-four times in the 44 cases, and in the remainder other signs, notably those of internal hemorrhage, were so marked that it was not noted in the history. Nevertheless, it is not an infallible symptom, as proved by 2 cases related by Baum. Riebel (Quarterly Bull. N. W. Univ. Med. School, Sept., 1910).

In reporting 3 cases of *laceration of the right coronary ligament* of the liver due to blows in the costal area on the right side, the writer gives the following diagnostic differential signs:

From a renal injury, by the absence of costovertebral tenderness, absence of blood in the urine; the pain is located by the patient more anteriorly in the flank and higher up than in renal injury. There are also signs of intraperitoneal irritation.

From a rupture of the liver bulk it differs only in degree; the symptoms are more active, collapse is added to

the shock, the abdomen is held more rigid, breathing is entirely costal, and the pulse continues to fail. M. R. Bookman (Med. Rec., Jan. 13, 1917).

Umbilical ecchymosis is regarded as a symptom of wounds of the liver by the writer. His case was one of thoraco-abdominal injury, associated with wounds of the lung and the convex surface of the liver, in which ecchymosis in the upper half of the umbilicus appeared. Bonnet (Lyon Chir., Sept.-Oct., 1919).

A rent is probable after a severe injury if there is collapse, if the pulse becomes more rapid and small, if the patient shows signs of exsanguinity, if the area of liver-dullness on percussion is increased, and if pain radiating to the scapular region is complained of. Severe injury may exist, however, without these indications.

Lesions of the Gall-bladder or Biliary Ducts.—Blows and other conditions capable of causing hepatic rents sometimes implicate these organs in the lesion. There may be severe pain in the right hypochondrium if a rupture exists, vomiting of food and bile, and icterus. The urine is usually dark-mahogany and the stools ash-gray in color. Tenderness over the hepatic region is usually marked. The intensity of the symptoms depend to a degree upon the quantity of bile voided into the abdominal cavity; but, this secretion being aseptic, peritonitis only occurs as a complication when the peritoneum is itself implicated in the traumatism, or when the lesion is at the junction of the biliary tract and the intestinal canal, the latter in that case acting as a source of infection.

In the diagnosis of injury of the liver bradycardia is a suggestive sign. In one case the liver had been rup-

tured by the kick of a horse and the pulse was only 48. In the other case the liver had been sutured and the pulse was 52. Several writers have mentioned bradycardia with injury of the liver, and ascribe diagnostic importance to it. The writer experimented on animals to determine the influence on the pulse of injury of liver and spleen. The results with 20 animals showed that bradycardia is a characteristic symptom of injury of the liver, but that its absence does not exclude injury of this organ. Finsterer (Archiv f. klin. Chir., Bd. xcv, Nu. 2, 1911).

According to Tilton hepatic injuries usually cause pain to radiate to the right shoulder. Inasmuch as there is also local pain on respiration, the chest does move as much on the right as on the left. This may lead to a misconstruction of the diagnosis, for it suggests to the casual observer thoracic injury. The blood gravitates into the right iliac fossa and may give well-marked dullness. Disappearance of liver dullness is due to beginning tympanites and is therefore not of great diagnostic importance. Jaundice is occasionally present, but usually does not appear until the second or fourth day. Ludwig found it 24 times in 267 cases. Its presence usually signifies injuries of the bile-duct.

Lesions of the Spleen.—The causes of injury to this organ are the same as those of the liver. Rents, sanguineous infiltration, and partial crushing are the lesions most frequently observed. Enlargement of spleen through a malarial cachexia renders it susceptible to lesions which traumatism would not give rise to were it in its normal state.

The malarial spleen seems particularly susceptible to rupture. The presence of a slow and strong pulse, after the phase of shock has passed off, does not exclude the possibility of a ruptured liver, since it is due to absorption of the biliary acids. Abdominal rigidity, the presence of an

intra-abdominal fluid collection, localized or radiating pain, are the main symptoms. H. Finsterer (Wiener med. Woch., July 6, 1918).

In extensive lesions copious hemorrhage usually takes place and death rapidly follows. If the lesion present is less severe, however, and the hemorrhage be moderate, there is tendency to collapse, increasing pallor, and a feeling of suffocation. The latter symptom and severe radiating pain in the region of the spleen are generally present, besides the signs peculiar to all abdominal injuries. If the patient survives sufficiently long the immediate effects of the traumatism, peritonitis or abscess and other complications frequently result. Severe local pain generally continues for some time, and chills are not infrequent. Percussion shows the organ to be more or less enlarged.

According to Trendelenburg, vomiting is a most important guide in the diagnosis of rupture of the spleen; in simple contusion of the alimentary tract it is very seldom if ever encountered.

> The symptoms of traumatic rupture of the spleen are essentially those of internal hemorrhage, and the diagnosis is usually not made until after abdominal section. The symptoms are obscure so far as enabling the distinction whether the spleen or some other abdominal viscus is ruptured. However, there should be no difficulty in diagnosticating the existence of hemorrhage into the abdominal cavity, and, when this condition is recognized, abdominal section is indicated. The incision should be made over the region of greatest dullness, if this can be determined. If percussion elicits a note of higher pitch in one flank than in the other, a valuable hint as to the source of hemorrhage has been obtained. Should the hemorrhage be sufficiently severe to give a percussion note of equal dullness in all regions the indication is to make the incision in the middle line. The treatment is essentially surgical, the object being the control of hemorrhage, and all authorities are agreed that this end is most certainly accomplished by splenectomy. The mortality following removal of the healthy spleen for rupture is about 40 per cent., whereas that of non-operative treatment is probably 100 per cent. Watkins (Med. Rec., Mar. 14, 1908).

> Case of a man who fell over an obstruction, got up and walked a few steps, but was then seized with pains in the left thoracic base region. On examination his pulse was only slightly weakened. Beneath the left costal border there was some degree of muscular resistance. The pains continued and became more violent. Later his appearance grew worse and the abdomen became rigid. A diagnosis of intraperitoneal hemorrhage probably due to rupture of the spleen was made, and the patient operated upon. The abdomen was full of blood and the spleen separated into 2 distinct parts by a rupture perpendicular to its major axis. The pedicle was ligatured and the splenic cavity cleaned out. The postoperative course was simple. Examination showed that the rupture was at the union of the anterior and middle thirds; the capsule was largely denuded for about 3 cm. The author believes the rupture occurred in two stages: First, a parenchymal rupture with intrasplenic hemorrhage and formation of a subcapsular hematoma; secondly, upon an effort, capsular rupture and peritoneal inundation. Lefèvre (Presse Méd., p. 617, 1917).

Lesions of the Kidneys.—The kidney is firmly held in place by its attachments, while its consistence is such as to preclude elasticity. Hence, a blow or undue pressure may cause rupture. All the causes of injury that may take part in the production of lesions elsewhere may also induce

renal lesions, which may consist of contusion, rupture, or laceration.

The 2 salient symptoms in contused wounds of the kidney in war are hematuria and perirenal hematoma. The first is observed in 95 per cent. of the cases. Unless primary hematuria is abundant, expectant treatment may be observed.

Hematoma is of equal value with hematuria as a symptom. If it constantly increases, it indicates immediate operation which may otherwise be deferred. There is, however, danger of the hematoma becoming infected if no operation is done, and there is a second danger of fibrous coating being formed around the kidney which may prevent its functioning and giving rise to a chronic sclerous perinephritis. P. Nogues (Jour. d'Urol., vii, 123, 1918).

The hidden gravity of such cases is well shown by the case of a girl, 4 years old, who fell over backward while on a hobby horse, the saddle striking her directly across the abdomen at the umbilical level. The only immediate effect was slight pain and tenderness over the right lower ribs. On the second day the temperature rose to 103.5° F. (39.7° C.). The tentative diagnosis was either injury of an abnormally placed appendix or a hematoma of the abdominal wall. Although the acute symptoms then subsided, a mass appeared 1 week later below the free border of the ribs on the right side. This mass was very tender and painful and was thought to be the liver, either abscessed or containing a new-growth, or an encapsulated hematoma. It rapidly increased in size, and there was cardiac and respiratory oppression with progressive anemia. On the 36th day an exploratory laparotomy was done. The liver was found to be normal but entirely displaced by a large mass, which when opened was found to contain serum, blood and clots, and a few soft pale-gray masses resembling sarcomatous tissue of the small round-celled type. This mass proved to be the right kidney entirely disorganized and broken down, the tumor wall being the kidney capsule. The kidney was drained and packed.

Autopsy revealed a slight loss of cortical substance and contusion of the kidney capsule, allowing a slow but progressive hemorrhage to take place beneath and within the capsule. H. P. DeForest (Jour. Dis. of Children, xv, 273, 1918).

Besides the symptoms common to severe abdominal traumatism there may be increased pain in the lumbar region with radiations in the direction of the pubis and rigidity of the muscles. Dullness on percussion is sometimes elicited. Anuria may also occur, but this is not a characteristic sign. Hematuria is an important indication of renal laceration, however, although it may not present itself at once; it may be followed by the appearance of pus. The catheter should be used in these. Retraction of the testicles is also said to occur (Rayer). The ureter is very rarely involved; when it is, the symptoms are not modified. Enlargement of the lumbar and hypochondriac regions is present in the majority of severe cases, but may supervene late in the history of the case.

Thanks to the compensatory work of the uninjured kidney, the mortality of renal lesions is not so marked as when other abdominal organs are injured.

Even severe wounds have been known to heal. If large renal vessels are torn, marked lividity occurs, the patient rapidly becoming exsanguine. Death may thus follow very soon. Involvement of the peritoneum in the injury is promptly followed by peritonitis, the signs of this affection appearing a few hours after the

receipt of the injury. Sepsis is not an infrequent complication in un-operated cases.

> When a patient has sustained an abdominal injury, manifesting the usual symptoms of shock, a gradually increasing resistant swelling over the kidney region requires prompt surgical intervention. The operation should be performed within the first 12 hours after injury. The surgeon can discriminate between mild cases which need no surgical interference and those that manifest injury to the deep-seated organs. C. W. Roberts (Jour. Med. Assoc. Ga., vii, 81, 1917).

PROGNOSIS.—Death almost invariably attended rupture of the intestinal tract prior to the introduction of exploratory abdominal section, and prompt resort to active surgical procedures, when necessary, is indicated.

As to the liver, as late as 1864 wounds of this organ were considered as practically hopeless in every instance. While a very small proportion of these cases recover without surgical interference, as is shown by the scars occasionally found in the hepatic parenchyma, the fact remains that an exploratory laparotomy, permitting the surgeon quickly to arrest the loss of blood in case of hemorrhage and to rid the peritoneal cavity of accumulated extraneous fluids, has greatly reduced the mortality. The prognosis becomes much more unfavorable when peritonitis has set in, but a fatal issue may sometimes be averted, even in advanced cases of this complication, by surgical intervention.

The same remarks apply to rupture of the gall-bladder.

Slight contusions of spleen heal readily, but rents and tears of any importance are frequently followed by fatal hemorrhage. Abscesses occasionally complicate convalescence.

The great majority of cases of rupture of the kidney that recover are those in which the initial lesion had been comparatively slight. In the graver cases, in which there is copious hemorrhage into the perinephric tissues or into the peritoneal cavity, of which the growing exsanguinity of the patient is an indication, the prognosis depends upon the speed with which adequate surgical procedures are instituted. Occasionally, however, the blood is held in check by the renal capsule.

The prognosis depends greatly, therefore, upon the patient's ability to stand operative procedures suitable to establish a positive diagnosis and bring the lesion that may at any moment destroy life within the immediate reach of art's highest powers. When serious injury is rendered probable by the nature of the accident, and the symptoms present also indicate a serious lesion, an exploratory incision, if the patient is not past relief, a careful examination of the organs involved, arrest of hemorrhage, closure of the disrupted tissues, or cleansing of the abdominal cavity may save him even when his condition appears almost hopeless.

Again, the prognosis is influenced by the time elapsing between the accident and the institution of surgical procedures. The sooner they are resorted to, all things considered, the greater the chances of success.

No case can be considered as hopeless unless a subnormal temperature, cold and cyanosed extremities, and other signs indicate that the end is near.

Even when performed late in the

history of the case, adequate operative measures sometimes prove successful.

The mortality in injuries of the kidney is, under the best surgical procedures, about 30 per cent., according to Crawford. Death in these cases, if not immediate, as the result of shock, or hemorrhage, or injury to other important organs, is due (1) to anuria, (2) to infection, or (3) to secondary hemorrhage. Anuria is probably due to a reflex contraction of vessels in the sound kidney owing to stimulation of the splanchnics and the vagus endings (Masius). Secondary hemorrhage may not occur for a week or ten days after injury and is then due to a disintegration of blood-clots, which are acted upon by the urine. Infection may be (a) local, with deep cellulitis and subsequent general involvement; (b) peritonitis, or (c) an ascending involvement of the opposite kidney due to the breaking down of blood-clots in the bladder.

The early recognition of a rupture of the bladder greatly influences the prognosis. About 60 per cent. of the most unpromising lesion, intraperitoneal laceration, are saved by prompt surgical measures. The remaining 40 per cent. are unsuccessful mainly on account of delay in resorting to abdominal section. A favorable result has, nevertheless, followed laparotomy as much as fifty-four hours after the rupture.

TREATMENT. — Shock. — Shock or collapse, though unreliable as a sign of severe injury to the abdominal viscera, is, nevertheless, an alarming condition, especially if the temperature is subnormal and the breath is shallow, and it should at once receive attention. The patient is placed in bed with the **head low,** and a free supply of **pure air** insured, supplemented with **oxygen** if practicable. **Hot-water bottles** are placed around him and he is covered with blankets previously warmed, if possible, or wrung out of hot water.

Two main elements have to be borne in mind in this class of cases: (1) that the state of shock is due to a direct commotion of the sympathetic system with probable inhibition of the heart's action, and (2) the possibility of an internal lesion which may involve death by exsanguination or the outpour into the peritoneal cavity of gastric or intestinal fluids. While the first condition calls for stimulants adapted to sustain the flagging heart and restore the action of the vasomotors, the agents employed should not be administered by the mouth, since, in case of rupture of the stomach, the duodenum, or jejunum, a portion, at least, of the fluid may be added to those that may have found their way into the peritoneal cavity. **Rectal and subcutaneous injections** should be resorted to.

If no remedy be at hand, subcutaneous injections of 1 dram of **whisky** or **brandy** may be employed, and repeated every five or six minutes until reaction occurs. A **turpentine stupe** or a fresh **mustard poultice** (not plaster) over the xiphoid cartilage, and a **rectal injection** composed of a tablespoonful of turpentine, a raw egg, and a teacupful of warm water, sometimes act with surprising rapidity. Hypodermic injections of **ether,** or, better still, tincture of **digitalis** with $\frac{1}{120}$ grain of **atropine,** repeated in fifteen minutes, are necessary to sustain cardiac action. After the second dose the digitalis may be injected alone several times more. These measures are greatly assisted by **galvanic stimulation of the phrenic nerve,** the negative pole, moistened in a solution of chloride of ammonium,

being applied to the neck in the depression immediately in front of the sternomastoid muscle, and the positive over the epigastrium.

These means are sometimes inefficient and **hypodermoclysis** should be performed. If a fatal issue seems inevitable, **saline transfusion** is indicated.

Cases of abdominal wounds in more or less marked shock should receive at once a subcutaneous injection of 1 or 2 cg. (⅙ to ⅓ grain) of **morphine,** and then means be applied to increase the blood-pressure and vitality. **Camphorated oil** is given after the morphine in doses varying from 3 to 4 c.c. (48 to 64 minims), at most 2 c.c. (32 minims) being injected at the same point. **Adrenalin** is likewise given subcutaneously in doses of 1 or 2 c.c. (16 to 32 minims) of a 1:1000 solution. The saline may be administered hypodermically or intravenously. If the shock is very severe, the patient should rest for not over two hours, the stimulant being repeated at intervals. During the operation it is necessary to combat shock by repeating injections at intervals. Postoperatively the Fowler position is not indicated in all cases; some may require a lateral decubitus or even a horizontal position with the head pendent, especially when there has been abundant hemorrhage and threatening anemia. Food and all drink is forbidden for the first twelve hours. Then only a spoonful of milk and water, brandy, or wine with water is given every hour. To overcome meteorism enemas of equal parts of **warm water** and **glycerine** are personally administered by the physician. After expulsion of gas, the intestine is cleansed with warm **salt water.** W. Stoppato (Policlin., xxiv, sez. chir., 1917).

With reference to abdominal wounds in civil life, stress is laid on the increasing frequency with which preventable fatalities are observed from injury to intra-abdominal vis-cera accompanying external trauma without production of positively indicative local or general symptoms. It is the imperative duty of the surgeon to intervene provided there exists even presumptive evidence of internal damage. A properly executed **celiotomy** is practically devoid of clinical risk. Where visceral damage has occurred the mortality under expectant treatment is nearly 100 per cent. F. T. Fort (Internat. Jour. of Surg., Sept., 1920).

Report of a case of accidental shooting in which the bullet punctured the bowel 7 times and passed out of the abdomen at the side opposite of entrance. No attempt was made to evacuate the intestine. An incision was started at the point of entrance of the bullet and extended along its course for 7 inches. Each small hole in the intestine was repaired by inverting the ragged edges into the wound and closing with a double row of Lembert sutures, penetration of the mucous coat being avoided. A small drain of iodoform gauze was left in the wound until the bowels had moved twice. Prompt recovery followed. Vertner Kenerson (N. Y. Med. Jour., Sept. 7, 1921).

Report of a case in which an operation was performed 2 hours after a pistol wound of the right hypochondrium. A tunnel wound of the liver was found, and was controlled by **gauze** packing. The gauze was removed on the fourth day and recovery followed. Another case, in a girl of 12 years, was operated upon 6 hours after the infliction of wounds. Five perforations were found in the small intestine. These were **sutured.** A **cigarette drain** was left in the cavity, and removed in 2 days. Recovery took place. Charles Farmer (Ky. Med. Jour., Sept. 1921).

Reaction.—As soon as reaction occurs in these cases another danger threatens the patient, that of hemorrhage, which the state of collapse has so far prevented to a degree, unless an extensive injury has caused over-

whelming exsanguination. In this event, however, the patient's recovery from the preliminary shock would hardly have taken place. Hence the necessity of closely watching the sufferer.

Cases of prolonged collapse sometimes turn out to be trivial, while a short period of it may be the prelude to the most grave complications. The former cases are, unfortunately, rare, and profound shock of any duration should be looked upon with suspicion. This is especially the case when a second period of shock is passed through—the "relapsing collapse" of Bryant—indicative of a secondary hemorrhage or the giving way or separation of some damaged tissues.

> The condition after subcutaneous rupture of the abdominal wall may become very serious in a short time. Any surgical procedure instituted must be thorough, all intestinal lesions being repaired, bleeding points checked, and blood-clots, when abundant, all removed. For the peritonitis arising from fecal material in the abdominal cavity good **drainage** with tubes must be established, with **saline proctoclysis and hypodermoclysis,** enterostomy and **saline flushing of the bowel** for intestinal paresis, and repeated **stomach washing** for vomiting and gastric distention. Dardanelli (Rif. med., June 8, 1912).

That cases clearly showing by their history and the active symptoms a grave injury should be submitted to surgical measures as early as possible will hardly be gainsaid in the light of our present knowledge. An equally positive conclusion, based on every means of diagnosis available, will alone warrant the assertion that no serious injury is present; but, if on the other hand, doubt exists,

abdominal section will alone insure the patient adequate protection. If nothing be found, no harm will have been done if precepts governing aseptic surgery have been closely followed; if a rent in the liver, an intestinal tear or rupture, a serious hemorrhage be discovered and adequately dealt with, the patient will have received the benefit of all our art's resources.

The seat of rupture being located, the nature of the injury will determine the procedure to follow, linear enterorrhaphy being indicated in longitudinal ruptures, and circular enterorrhaphy in complete ruptures. These procedures are now generally preferred to an artificial anus. It is sometimes impossible to adjust adequately the edges of the wound, owing to the condition of the margin, and an omental graft must be used to cover the contused area so as to avoid a secondary perforation.

Considerable extravasation of feces, blood, and other liquid or semiliquid material may have occurred into the peritoneal cavity. All chances for further contamination of the intestinal tract having thus been removed by closure of the rupture, the peritoneal cavity should be carefully cleansed by flushing with warm, sterilized water, a soft aseptic sponge being employed to mop gently all the surfaces that may, in any way, have come in contact with the infectious fluids. The cavity is then closed and free drainage insured.

Satisfactory results are obtained even in cases in which very great injury and ample opportunity for infection of all wounds have markedly compromised the issue.

The after-treatment should be

based upon the necessity of insuring rest for the intestinal tract for a few days. This may be carried out by administering opiates. The patient's strength should be sustained by means of nutrient, but small and frequently administered, enemata.

Under all circumstances, an abdominal injury should cause the patient to be watched several days. After an uncomplicated injury he should remain in bed and be placed on a milk diet for a few days. **Anodyne applications** over the abdomen and a little **morphine,** internally, if there is pain, is all that is usually required in these cases. In the less fortunate the procedure to be adapted varies according to the organ involved.

Intestines.—The probability of a rupture having been recognized, the abdomen should be opened by an incision through the linea alba, and any hemorrhage quickly arrested.

The next step is to locate the visceral injury. Of importance in this connection is the fact that in the majority of cases the rupture is due to compression against the spinal column. The spot over the abdomen · upon which the blow carried being considered as the one end of an imaginary line and the center of the vertebral column as the other end, the probabilities are that the rupture will be found near the linear axis.

Again, if the rupture cannot be readily found, hydrogen may be gently insufflated into the rectum, as advised by Senn, and the spot from which the gas escapes will indicate the location of the rupture,—approximately, in the case of the small intestine, and accurately below the ileocecal valve.

Disorders, or lesions other than those sought after, are misleading conditions that should be borne in mind.

Lesions of the jejunum are sometimes difficult to locate.

Stomach.—When the symptoms of complete tear are recognized, the presence of the organ's contents in the abdominal cavity render an immediate laparotomy imperative. The incision should include the tissues between the xiphoid cartilage and the umbilicus. If the tear cannot be quickly found, repetition of the inflation with hydrogen-gas will help to locate it. As soon as located any bleeding vessel should be ligated, and the stomach evacuated and cleansed through the adventitious opening of any substance that may have remained in it. If the wound be a lacerated one, it may be necessary to pare its edges. This being done, the tear is closed, the mucous membrane being united with a continuous or interrupted suture, cut short, and the muscular and serous coats by the continuous Lembert suture. Closure of the laceration having removed all danger of further extravasation into the peritoneal cavity, the latter must be flushed with warm, sterilized water and mopped out with a soft sponge. The cavity is then closed and a drain left if the peritoneal surfaces have been exposed to contamination for some time.

Liver.—Especially when the history of the case seems to indicate the possibility of a lesion of this organ is careful watching imperatively demanded, owing to the violent hemorrhages which they involve. Either this complication or peritonitis having been recognized, the abdomen should
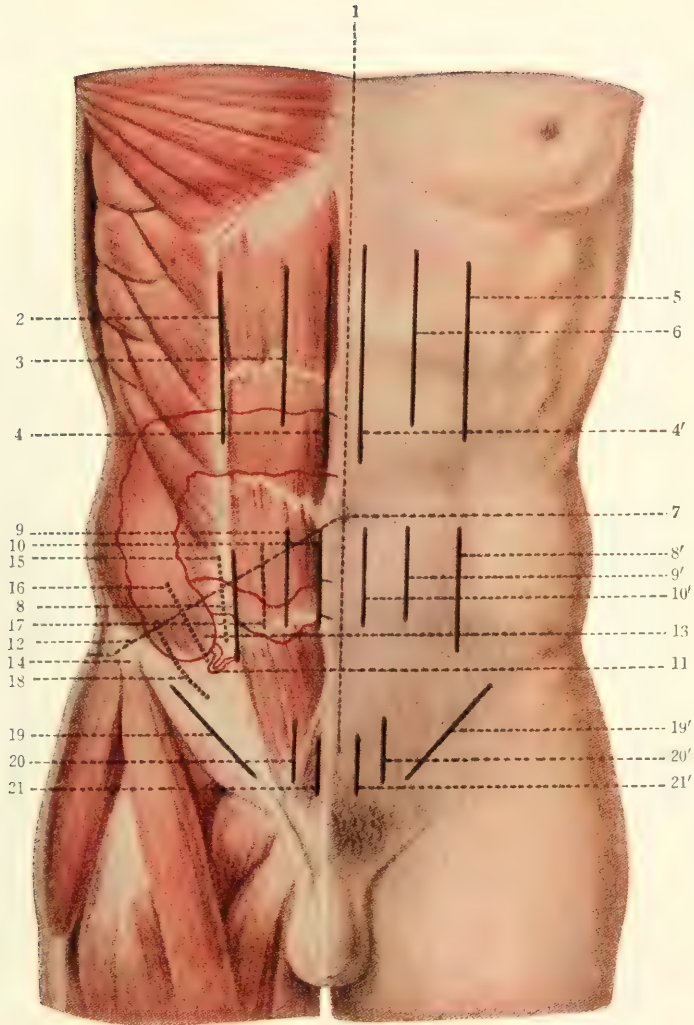
Lines of Incision for Abdominal Exploration and Operation (Laplace).

1, median line; 2, for liver and gall-bladder; 3, for pyloric end of stomach and duodenum; 4, 4', for upper abdomen, including stomach and pancreas; 5, for spleen; 6, for tail of pancreas or greater curvature of the stomach; 7, umbilicus, median line; 8, 8', 9, 9', 10, 10', for intestines according to location of injury, 8 being the best for appendix as it severs no muscular fibers; 11, vermiform appendix; 12, McBurney's line; 13, cecum and ileum; 14, anterior superior spinous process of the ileum; 15, 16, 17, 18, defective incisions for appendicitis: they cut across deep muscular fibers; 19, 19', for inguinal hernia; 20, 20', 21, 21', for bladder according to location of injury.

be opened at once in the middle line. The abdominal wound should be large enough, if possible, for the surgeon to see the liver, but in every case he ought to make a careful exploration with his finger, especially directing his attention to the convex and posterior surfaces of the organ.

When a rupture is found, the wound may either be cauterized, plugged, or sutured.

Plugging with antiseptic or aseptic gauze seems to give the best results, one end of the gauze being left out at the angle of the abdominal wound. The plug should be removed not earlier than the forty-eighth hour, lest there should be a recurrence of the hemorrhage, and not later than the fourth day, lest a biliary fistula should be formed. When the bleeding is very severe, sponges mounted on holders appear to produce more satisfactory pressure than simple plugging, which is, perhaps, better reserved for slighter injuries. Hot-water irrigation may be of advantage in these cases. A ligature should be applied to any large vessel which is seen to have been torn. Sutures are particularly useful when the laceration extends deeply into the substance of the liver, since by their means the edges of the wound may be brought lightly together and the bleeding can be controlled. Drainage of the pelvic pouch, by an opening just above the pubis, serves best to give free passage to subsequent discharges. The capsule should be included in the stitches. The prognosis is very unfavorable when peritonitis has occurred, but something may still be done to prevent the fatal issue by opening and afterward draining the abdominal cavity.

In **suturing** the liver, the writer passes the needle, threaded with catgut, through a small wheel made of fine silver wire. Each wheel, the diameter of which varies from 6 to 15 mm., has 8 spokes. A. L. Soresi (Riforma Medica, Mar. 2, 1917).

In a case of traumatic rupture of the liver in a boy, aged 8 years, due to being run over by an automobile, the outstanding signs were the thoracic type of breathing, the anxious expression, and the history of severe trauma. Normal urine was voided. When there is a possibility of a solid abdominal viscus being damaged, it is generally safer to **explore at once** rather than await the symptoms of hemorrhage. Doyle (Med. Jour. of Australia, Jan. 10, 1920).

Spleen.—After a simple contusion the spleen soon returns to its normal condition without further trouble, and a few days in bed, coupled with strapping of the side to limit motion, usually suffice. When, however, there is laceration of the parenchyma the convalescence is slow, abscesses following in quick succession. After a time these cease and recovery is uninterrupted. Symptomatic treatment, revulsion over the organ, and tonics may shorten the duration of such cases.

When the symptoms do indicate that exsanguination of the patient is taking place, death will most probably follow, although the hemorrhage is not as copious as it can be in tears of the liver, the splenic capsule being more elastic than that of the latter organ. Removal of the organ should be resorted to. The abdominal wall is opened by means of an incision through the left semilunar line and the peritoneum is freely opened. The hand being introduced into the cavity, all adhesions are torn up and the organ is brought to view. The

vessels entering the hilum are then clamped and the organ is removed. The stump is ligated and, after sponging out the abdominal cavity, the wound is closed.

> Summary of cases of rupture of the spleen reported in literature: Unoperated: Of 220 cases, 17 patients recovered—mortality, 92.3 per cent. Operative results: Splenectomy, 67 cases, 38 patients recovered, 29 died —mortality, 56.7 per cent.; splenorraphy, 2 cases, 1 patient recovered, 1 died—mortality, 50 per cent.; tamponade, 6 cases, 5 patients recovered, 1 died—mortality, 83.3 per cent. In the splenectomies, 13 patients had complicating injuries, of which 9 died. In 2 which recovered, the complications were unimportant. Ross (Annals of Surg., July, 1908).

Kidney.—The majority of mild cases of perirenal extravasations of blood and urine recover as the result of rest and expectant treatment. The patient should be kept in bed and his diet limited to liquids, the best of which is milk; this beverage requires, besides, the least physiological labor from the injured organ. The nourishment of the patient may further be sustained by rectal injections of beef-tea, and these should entirely be resorted to if there is vomiting, the latter tending greatly to encourage hemorrhage.

> Details of 5 cases. The patients were men between 25 and 42, a woman of 30, and a boy of 12. Unless there are signs of internal hemorrhage, absolute repose and ice to the kidney region are indicated. The patients were all dismissed in good condition after operative intervention. Yoshikawa (Beiträge z. klin. Chir., Jan., 1909).

When hemorrhage occurs in the direction of the bladder, there is likely to be accumulation of blood-clots, which, if small, will readily pass out with the urine. Frequently, however, the clots are large and cause retention of urine and marked tenesmus. A large catheter should therefore be introduced and kept *in situ* when the hematuria is marked, and the bladder occasionally washed out with a weak **boric acid solution**. Median urethrotomy to remove clots and relieve retention sometimes becomes necessary in these cases. When the symptoms do not improve under these measures, an incision should be made, exposing the seat of injury, the extravasation removed, and the parts restored to their normal conformation.

According to Keen, hematuria is valuable only as showing the fact of rupture of the kidney, but not as a symptom by which to decide on operating. It is not the visible loss of blood by the bladder, but the easily overlooked, but far from dangerous, bleeding into the perinephric tissues, or into the peritoneal cavity, that should receive the chief attention.

The dangers of rupture of the kidney are mainly hemorrhage and sepsis. When, therefore, the symptoms are such as to indicate marked hemorrhage or sepsis, and especially if a tumor form quickly in the lumbar region, an exploratory operation should at once be done. If severe laceration be present, or the kidney's functions be practically compromised, or the hemorrhage be such as to require ligation of the renal vessels, lumbar nephrectomy should immediately be performed, primary nephrectomy being safer than secondary removal of the organ.

> When hematuria continues and a hematoma forms in the region of the

kidney which seems to be increasing in size, and when there are symptoms of concealed hemorrhage, it is far better to operate then under good conditions than to wait until the risk is greatly increased. Even if the hematoma does not appear a hemorrhage may be dissecting up tissues for a considerable distance, and then the evidence of concealed hemorrhage must take the place of evidence of a hematoma. The danger of an exploratory operation is not great if it is undertaken before too extensive hemorrhage or septic infection has taken place. Frank Walker (Boston Med. Surg. Jour., May 24, 1917).

Bladder.—When a patient presents the history of a severe abdominal contusion or crushing, followed by inability to micturate, the catheter should at once be used.

The presence of hematuria will indicate a lesion in the urinary tract, kidney, or bladder. If the urine withdrawn is observed to be well mixed with blood and, instead of red, it appear brown and smoky, the lesion is probably one of the kidney. If, on the contrary, the urine be bright red, the probability is that the bladder has been torn. In the latter condition the diagnosis may also be assisted by the quantity of fluid passed at a given time. If, when the catheter is introduced and after a history marked with shock, no urine is obtained, the chances are that not only the bladder has been ruptured, but that the laceration is extensive, the opening having allowed the vesical fluids to escape into the abdominal cavity. A free flow, on the contrary, would tend to show that the tear, if any exist, is small. Of course, the invagination of the intestines into the vesical opening, or a valve-shaped laceration, may cause the same favorable signs to exist, thus misleading the diagnosti-

cian. Very small lesions may be present, sufficient to allow the urine to escape, drop by drop, into the surrounding parts. Detection of them is very difficult, the subsequent complications alone showing the presence of extravasated fluids.

The presence of any tear, except very small ones, may also be ascertained by injecting a weak boric acid solution into the organ, through the catheter. If a rupture be present, the bladder will not fill and rise above the pubis. Filtered air may be used for the same purpose, but it is less satisfactory, owing to the danger of secondary collapse.

The urine may have passed into the prevesical connective tissue outside the peritoneum, or the vesicorectal or vesicouterine space, owing to a rupture in these locations. This constitutes the extraperitoneal lesion. Cellulitis and sloughing rapidly ensue without subsequent involvement of any organ in the neighborhood of the lesion, the vagina, the rectum, etc., the patient dying from septicemia.

Death in intraperitoneal rupture of the bladder is due in a majority of cases to uremia and not to peritonitis. In most instances death occurs before the latter can develop. One should operate whenever there is suspicion of intraperitoneal rupture and not wait for evidences of a peritoneal reaction. Rost (Münch. Med. Woch., Jan. 2, 1917).

To ascertain whether a tear be extraperitoneal or not, a measured quantity of a weak boric acid solution is injected through the catheter. If the full amount is not recovered, the chances are that the rupture is extraperitoneal.

Report of a case of traumatic rupture of the bladder in which an un-

usual feature was the obtaining of urine in considerable quantities after catheterizing the patient. The patient had been kicked on the lower abdomen. The house surgeon passed a catheter and obtained about 10 ounces of blood-stained urine. Eight hours later 16 ounces of urine were drawn off. The bladder was washed out with boric solution, the solution returned being apparently the same in quantity as was injected. L. Gordon (So. Africa Med. Rec., Feb. 28, 1920).

Rupture into the peritoneal cavity, the intraperitoneal form of lesion, is less urgent as far as symptoms go. One, and even two, days may elapse before active symptoms appear; but, when they do, rapid progress toward a fatal issue from general peritonitis is the rule.

Uncomplicated contusion of the bladder readily yields to a few days' rest, the application of ice, and general symptomatic treatment. When, however, there is cause for suspecting a rupture from the nature of the accident or the violence of the blow, the catheter should at once be introduced. The presence of blood renders operative interference imperative. After the rectum has been distended with a rectal bag an incision three inches long is made in the middle line of the hypogastrium, beginning half an inch below the upper edge of the pubes, as in suprapubic lithotomy.

The peritoneum is then carefully rolled up, along with the prevesical fat. The bladder being thus exposed, search for the rupture is the next step. The rent is usually found along the posterior surface vertically down from the urachus; frequently an extravasation of blood and urine indicates the spot. Occasionally, however, considerable difficulty is

experienced, and opening of the organ is necessary so as to permit the introduction of the finger, and thus allow of exploration of its inner surface.

The rupture may be extraperitoneal or intraperitoneal. If an intraperitoneal laceration is found, the incision should be extended upward, the peritoneal cavity opened, and the cystic wound closed with fine silk by means of Lembert sutures, one-eighth of an inch apart, including only the peritoneal and muscular coats. The mucous membrane of the bladder should be respected. Important, in this connection, is the necessity of ascertaining that the sutures will hold; this may be done by distending the bladder with a lukewarm milk or an alkaline solution.

The abdominal cavity is then carefully irrigated and closed, leaving a drain if there is any possibility that fluids will accumulate in any of the surrounding tissues.

Henry Morris holds that there is great danger in delaying operation in these cases; the decomposition of the clots and the cystitis which is excited by their presence, as well as the frequent catheterization needed, exposes the patient to all the dangers of suppuration of the wounded kidney, and also to the risk of infection.

Patients who recover from extraperitoneal rupture are more apt to suffer permanent disability than those who recover from intraperitoneal rupture, chiefly because of the urinary extravasation about the base of the bladder, inducing infection, necrosis, and loss of function.

The treatment consists in drainage of the bladder either infra- or suprapubically. Suture of the bladder tear is of less importance in extraperitoneal cases. For an associated pelvic

fracture open operation wiring, etc., are unsatisfactory because of urinary infiltration. Indirect fixation by external screws and clamps was found useful in a boy of 16, injured in a runaway. A Freeman's screw placed on either side of the symphysis pubis held the pubes in apposition until fibrous union was well established. The total mortality in all varieties of ruptured bladder treated surgically since 1900 has been less than 25 per cent. E. P. Quain (Surg. Gynec, and Obstet., xxiii, 55, 1916).

Case of a man who had been kicked in the abdomen and jumped upon while intoxicated. The abdomen was rigid as in perforated duodenal ulcer; temperature, 102.5° F. (39.1° C.); pulse, 100 to 110. Three ounces of clear urine had been passed. Upon incising the peritoneum there was a gush of blood-stained fluid, possibly 2 quarts. A tear in the bladder from the space of Retzius down to the trigone was found. The balance of the fluid was aspirated from the abdomen and the operation concluded by suturing the rent in 3 layers, No. 1 chromic catgut being used first in the mucosa, the second layer including the muscular and serous coats and last the serous. A drain was placed in the pelvis and a catheter introduced through the urethra and fixed with a suture through the corpus spongiosum. The patient was placed in bed in the Fowler position with a Murphy drip. He was out of bed and voiding 16 ounces at a time on the tenth day. Erdman (N. Y. Med. Jour., Oct. 13, 1917).

Case of a man struck in the lower part of the abdomen by the pole of a wagon. The symptoms continued for nearly five days before he came to the hospital. Temperature, 100° F. (37.8° C.); pulse, 132; respiration, 32; white blood cells, 15,000; polynuclears, 73 per cent. The abdomen was opened and 130 ounces of fluid obtained. A small transverse tear found in the upper portion of the bladder was sutured and the bladder drained below the peritoneum through a stab

wound; the abdominal wound was also sutured and drained. Recovery was uneventful. E. F. Kilbane (N. Y. Med. Jour., Oct. 20, 1917).

In retroperitoneal intestinal rupture from contusion operative treatment is especially difficult. In 37 cases of retroperitoneal rupture in the literature, 29 cases were treated surgically, but in only 15 was the rupture discovered at operation. The surgeon may consider the condition due to retroperitoneal hemorrhage and close the abdomen with fatal results. **Suture,** though difficult, can be done with hope of success in selected cases. G. Soederlund (Nordiskt med. Arkiv, li, No. 5, 1919).

WOUNDS OF THE ABDOMEN.
—Wounds of the abdomen may be *non-penetrating,* when the abdominal walls alone are injured, and *penetrating,* when the peritoneum is included in the lesion, irrespective .of the instrument (pistol, knife, etc.) with which the lesion is produced.

Non-penetrating Wounds. — Non-penetrating wounds are usually due to pointed cutting or blunt instruments.

The lesions caused by a pointed instrument, involving the skin and muscles only, are usually very slight. With due aseptic precautions careful exploration of the wound with the finger may be resorted to if the visual examination does not suffice. Probes had better not be used, lest the wound be transformed into a penetrating one.

Lesions caused by cutting instruments (knives, swords, etc.) vary in importance according to their depth and length. When the muscles are cut, the support for the abdominal organs is compromised, and ventral hernia may follow, unless great care be taken when the wound is closed.

Lesions caused by blunt bodies

(such as shot, glancing bullets, and fragments of shells, etc.) are usually attended by symptoms of contusions corresponding in intensity with the force of the blow. Severe laceration of the abdominal tissues may thus be caused and death occur from intestinal lesions.

The hemorrhage attending these various kinds of wounds is usually slight. There is considerable ecchymosis, but this soon disappears. Occasionally shots or bullets become imbedded in the abdominal tissues.

The best sign of coexisting injury to one or more abdominal organs is rigidity, coupled, if there is abundant hemorrhage, with a small pulse, pallor, a pinched facies, and vomiting. Even slight abdominal trauma may entail severe symptoms, which, however, gradually decrease in intensity, whereas if actual organic injury has been occasioned, their intensity continues to increase. H. Riedel (Deut. med. Woch., Jan. 11, 1912).

The writer lays stress on transmission of the cardiac and respiratory sounds, so that they are audible over the whole abdomen almost as well as over the chest, as a sign of internal injury and positive indication for immediate laparotomy. This sign may already be present one-half hour after the injury, never exists in extraperitoneal injuries, has no relation to rigidity, and is ascribed to irritation of the parietal peritoneum through the outpouring of foreign material into the abdominal cavity. Claybrook (Surg., Gynec., and Obstet., Jan., 1914).

Visceral extraperitoneal wounds showed symptoms more marked, lasting, and alarming than parietal injuries. The symptoms giving the impression of peritoneal penetration are: dullness over the liver, muscular rigidity of all or part of the anterior wall, vomiting, small pulse, facies abdominalis, stoppage of flatus and feces which persists more than twenty-four hours, retention of urine, and traumatic shock. Any one or more of these signs may show in an abdominal wall injury, but the occurrence of all together is rare. Before the war any of these symptoms would usually have been considered indicative of intraperitoneal penetration. Tympanites was observed in 56 per cent. of the writers' series of extraperitoneal wounds. Stassen and Voncken ("Le péritoine en chir. de guerre," Paris, 1917).

It is sometimes impossible without a laparotomy to tell whether a gunshot wound of the abdomen involves the peritoneal cavity or not, for the signs and symptoms are not constant. It is first necessary to determine if possible the direction of the track. The absence of an exit wound does not necessarily mean that the foreign body is lodged in the abdomen. The facial expression is usually one of anxiety. Pain is not of great value, and may or may not be present. Tenderness is a very constant and reliable sign. Rigidity, or the absence of it, is often most misleading. The pulse increases directly with the gravity of the intraperitoneal lesion, and gives an important basis for prognosis. Vomiting is usually present, but not necessarily. Thirst is a most distressing symptom. Rœntgen-ray localization affords the most useful guide in the diagnosis of penetrating wounds. Operation should not be undertaken before the patient has recovered from shock. In patients with shock and hemorrhage the author has often waited six hours or more, taking the risk of further hemorrhage, with results that justified the delay. Provided the patient is warm, operation is done at once, saline being given while he is on the table. Charles (Brit. Med. Jour., Mar. 23, 1918).

Treatment.—After carefully arresting bleeding, cleansing, and disinfecting the wound, the tissues are united. In deep incised wounds the prevention of ventral hernia should

be borne in mind, and the cut muscular tissues brought accurately together by means of catgut sutures. This being done, silk sutures are also introduced and brought out to the surface, thus including the muscles and skin. Capillary drains are alone to be used, if drainage is at all necessary, larger drains affording opportunity for the formation of a ventral hernia. The abdomen should be supported by means of a bandage applied over the dressing and the patient kept in bed until complete repair of the wound has taken place; from two to five weeks, as a rule. The bandage should be carried long after recovery, and the patient be warned of the danger he might incur by violent movement or strain.

Penetrating Wounds.—The softness of the tissues of the abdominal parietes causes them to be easily penetrated, and the organs within the cavity are all vulnerable for the same reason. The interstices between them occasionally allow the harmless passage of a weapon or bullet, but such cases are extremely rare.

The missile may graze the peritoneum and barely miss it along with the deeper organs. Unfortunately wounds causing laceration of one or more of the abdominal viscera are the most frequent, and their fatality is proverbial unless a timely diagnosis allow of prompt protective measures.

As is the case in contusions, the direction from which the missile or stab comes is of great importance. A bullet arriving from the side and striking near the linea alba would probably create a buttonhole wound or bury itself in the abdominal walls. A bullet coming from the front, on the contrary, would most probably perforate the organs in its axial line of flight. If the bullet has passed through the body an imaginary line between the entrance and exit will probably indicate the organs injured, including, of course, the peritoneum. Here again, however, the spinal column may cause deviation when the initial velocity of the bullet is small, and a deceptive line of injury furnished. To positively determine the course of a bullet is difficult in many cases.

In stab wounds the opening is frequently of a sufficient size to permit prolapse of the omentum: an evident proof that the abdominal cavity has been penetrated. This rarely occurs in bullet wounds unless a large projectile, or a bullet coming from either side of victim, has caused comparatively large solution of continuity of the tissues. Prolapse of the omentum is most frequently observed in lesions of the left side. Coils of the small intestines are also frequently prolapsed and, in rare cases, the stomach, the liver, or the spleen has appeared between the lips of the wound.

Symptoms.—As is the case after contusion, penetrating wounds of the abdomen may give rise to no symptoms capable of affording any reliable clue to the extent of the internal injuries. Profound shock may be present and no serious lesion exist.

Severely injured individuals may, on the contrary, present no acute symptoms and, perhaps, walk or ride a considerable distance before showing noticeable evidence of their condition.

Profuse hemorrhage alone gives rise to symptoms denoting a grave lesion: rapidly progressive exsangui-

nation or acute anemia; nausea or vomiting; weak, rapid, and some-times irregular pulse; dilated pupils; cold sweats; yawning, ending in con-vulsions and coma. Shock is likely to be progressive in these cases.

The only symptoms that are present in practically all cases are pallor and vomiting: the accompani-ments of any severe blow on the abdomen, and therefore of no value whatever as differential signs. The temperature is of no assistance in these cases.

> The amount of "knock-out" after injuries such as will cause prolapse of the intestines is often surprisingly slight, subjects sometimes walking a considerable distance with such in-juries, with their intestines supported by a bandage. A man hit in the ab-domen may be quite unconscious that his intestine is prolapsed. Small mis-siles penetrating the bowel may cause very little immediate pain or disturb-ance; on the other hand, some men shot in the abdomen, or even the limbs, with a bullet or other small projectile, experience a tremendous blow or kick which may induce un-consciousness. Intense pain occur-ring promptly in wounds of the lower abdomen is especially connected with penetrating buttock wounds, and is valuable in calling attention to their dangerous nature. Apart from very extensive injury, the shock in abdom-inal wounds seems due, in great part, to loss of blood and, later, peritonitis. Some superficial lesions on the outer surface of the liver seem, however, to cause extreme shock, sufficient to cause death without marked blood loss. Stripping up of the retroperi-toneal tissue by blood causes dispro-portionate collapse, possibly on ac-count of sympathetic injury. A small injury causing great pain will produce pallor and collapse with cold extremi-ties, though the pulse be quiet and good. Cuthbert Wallace (Pract., Sept., 1916).

DIAGNOSIS.—On general prin-ciples dangerous complications are to be expected when marked shock, nausea, vomiting, hiccough, anxiety, intense thirst (indicating a probable involvement of the peritoneum), and insomnia are present. Besides these indications there are others peculiar to each organ which greatly assist in establishing at least an approximately certain diagnosis.

Intestines.—Bullets striking antero-posteriorly rarely cause more than four perforations, while oblique or transverse shots are likely to produce a much larger number of lesions: from fourteen to sixteen. On general principles, however, a penetrating wound may always be considered as having caused a lesion of the intes-tines.

The most important symptom is the escape of intestinal gases and more or less fluid substances through the wound. The mere presence of emphysema around the wound is of no value, however, since air is gener-ally forced into the wound by the bullet.

> The most experienced surgeons oc-casionally find more or less difficulty in diagnosing penetration and perfor-ation before operation, and all are, of course, opposed to precocious operating in non-penetrating wounds. An aperture of exit is not always present. Any missile may ricochet, and the writer has seen wounds in which, if the missile had traversed by the shortest route between the two openings, there would have been per-foration of many vital organs and structures; yet there was no serious injury.
>
> There are a few recognized rules to follow: The closer together the wounds of entrance and exit, the less the chance of penetration. According to Rochard, if there is persistent com-

plaint of abdominal pain, perforation is almost certain; if a patient passes gas at the anus, there is no perforation. Eastman (Amer. Med. Assoc.; N. Y. Med. Jour., Jan. 15, 1918).

Pain is usually one of the first and most constant signs of injury to the abdominal contents, its character depending upon the amount of fluid escaping into the peritoneal cavity. Associated with pain is spasm of the abdominal muscles, especially the recti, which, even though slight, can usually be detected. Patients operated upon while in shock nearly always die, while in cases of active hemorrhage they will die if not operated. The history and examination of the blood will help in the diagnosis, a leukocytosis being found in hemorrhage but not in shock. McGuire (N. Y. Med. Jour., Sept. 21, 1921).

Free hemorrhage from the wound tends to indicate an intestinal lesion; if the stools also contain blood the diagnosis may be considered as certain.

Probes have been discarded in penetrating wounds, owing to the irregular course followed by the bullet in many cases and the danger of creating a false passage. Digital exploration of small wounds furnishes but little information, while in bullet wounds there is danger of pushing into the peritoneal cavity what foreign substances may happen to be present.

The majority of surgeons now favor enlargement by an incision at least two inches in length, intersecting the bullet or incised wound. Layer after layer of tissue is carefully dissected on each side of the track, the walls of which, in gunshot wounds, are usually darker than the normal tissues, owing to contact with the lead or powder-products of combustion. Using the grooved director to divide the tissues and the hemostatic forceps to grasp any bleeding vessel, the peritoneum is finally reached, when the certainty that a penetrating wound is present or not may be established. If practised with strict aseptic precautions this procedure does not expose the patient.

War injuries of the large intestine are serious from their infectivity rather than their multiplicity. They are often more difficult to find and repair than those of the small gut. In war, many extensive tears are caused by shell fragments, but a bullet may itself completely divide the intestine, as witnessed by Wallace in the case of the ascending, transverse, and descending colon, though not in the case of the pelvic colon. Many wounds are extraperitoneal or partly extra- and intra- peritoneal at the line of reflexion of the peritoneum of the colon. The latter variety of wound is often overlooked, in spite of careful search, and if found, is very hard to suture adequately.

Stomach.—Hematemesis is a frequent symptom of penetrating wound of this organ and a much more valuable one than in contusion, since, in the latter, a slight laceration of the mucous membrane may produce it. The blood may be pure, but in the majority of instances it is mixed with partially digested alimentary semi-liquid material. If the wound is sufficiently large to allow the contents to escape through it the nature of the injury is, of course, clear, but an important complication is to be apprehended: extravasation into the peritoneal cavity capable of causing peritonitis. If this is circumscribed, adhesions are formed and the patient recovers. Frequently, however, gen-

eral peritonitis follows, ending in death. Hence the importance of an early recognition of extravasation.

Besides hematemesis and the presence of gastric fluids, there are usually present in such injuries the marked symptoms witnessed in cases of contusion: rapidly progressive anemia, pallor, fluttering pulse, etc.

> Gastric wound cases show pain, sickness, collapse, abdominal rigidity, and tenderness, vomiting being especially pronounced, but the collapse less marked than usual. The respiration rate increases more rapidly in proportion than the pulse rate. Pain is worst when the pyloric or cardiac ends are involved, and collapse most marked in wounds of the curvatures. Fraser and Bates (Brit. Med. Jour., Apr. 8, 1916).

> The writer cites 2 instances in civil life where a single bullet made 3 perforations in the stomach. This is due to the 3 contraction waves, each of which becomes quite deep as it passes toward the pylorus, thus making it possible for a bullet to graze or even perforate the tip of an inverted crest as it passes through. N. Kerr (Ills. Med. Jour., xxxiii, 267, 1918).

Liver.—A wound of the liver gives rise to all the symptoms observed when a contusion has caused laceration of the organ: Intermittent pain, radiating in various directions, especially toward the shoulder, if the convex portion of the organ is torn, and in the direction of the waist, if the concave or inferior portion of the organ is the seat of injury. There is marked pallor, superficial itching, and, later on, jaundice. The stools may be clay-colored, thus indicating the absence of bile.

The hemorrhage varies in these cases according to the cause of the lesion; one caused by a bullet is prone to be accompanied by considerable and frequently fatal bleeding. Stab wounds, when the weapon is not large, do not give rise to considerable hemorrhage. A copious flow of blood from a wound in the hepatic region indicates that the liver is involved. The flow of bile through the wound is a valuable sign, but it is seldom that this secretion can be obtained alone, blood being usually mixed with it.

Of 25 cases of hepatic injury occurring in New York hospitals, uncomplicated by serious lesions of other abdominal organs, 12 were ruptures, 9 gunshot wounds, 4 stab wounds. Eleven deaths resulted—a mortality of 44 per cent. (Tilton).

> Among 37 cases, the course of the missile was transverse in 21. Simple furrows often cause more troublesome hemorrhage than perforating wounds. Shell wounds, usually extensive, often cause secondary hemorrhage, and are nearly always badly infected, necrosis and sloughing of a great part of the liver following, as a rule. With an open shell wound suppuration is the rule, but is of no great importance. Secondary abscesses, however, are a grave matter. Of the 37 cases, 25 showed complicating pleural injury; next came injuries of the stomach. Seven cases showed no physical signs of liver injury. Secondary bleeding (4 cases) usually occurs about the tenth day and always means septic infection, which causes pain, distention, fever, and rapid, weak pulse. Twelve cases showed jaundice. Some form of biliary fistula—the most characteristic sign of liver injury—was present in 15 cases, opening through the pleura in 7, all of which recovered. Of 25 deaths from hepatic injury, 60 per cent. were due to sepsis and 40 per cent. to secondary hemorrhage. The chief lethal complication was hemothorax; 7 cases died from infection

from the effusion. G. H. Makins (Brit. Jour. of Surg., iii, 645, 1916).

In some instances extensive lacerations of various organs may give rise to no preliminary morbid phenomena. Thus, W. L. Robinson reported fatal cases of marked laceration of liver and bowel in which there was neither shock, hemorrhage, nor high pulse.

Spleen.—In cases in which the spleen is wounded the diagnosis can easily be established by the location of the external opening and the direction of the track. As is the case in contusion, there is marked local pain and profuse bleeding, which, if the organ is greatly lacerated, may soon prove fatal. This is apt to occur after gunshot wounds at close range, the organ under such circumstances becoming pulpified. Puncture wounds are less likely to produce fatal hemorrhage. Pain in the left shoulder has been considered a diagnostic sign of value.

The diagnosis of splenic wounds is always difficult. Almost never, in the first few hours after the injury, is there the least sign of bleeding, unless there is a crushing injury with tear of the pedicle, causing death within a short time. On the second to the sixth day, as a rule, the pulse suddenly becomes frequent and weak, signs of anemia become marked, and the subject unexpectedly succumbs. Dullness in the splenic region or lower in the abdomen due to blood is inconstant and difficult to make out. Some splenic wounds exhibit symptoms of peritonitis. The diagnosis is best based on the nature, site, and direction of the wound. Radioscopy is significant if it reveals a foreign body that has penetrated to a depth of 7 to 12 centimeters from the posterior wall. Even in doubtful cases celiotomy is indicated, with splenectomy whenever practicable. J. Fiolle (Paris méd., Aug. 25, 1917).

As a rule, injury of the spleen can be merely suspected, as tears of the liver, pancreas, and mesentery often present the same symptoms. The general signs of internal abdominal injury are not, as a rule, well marked at first. A slight hematuria, due to simultaneous slight injury of the left kidney, may help in the diagnosis.

It is better to operate once too often than once too late. The best incision is the median, for in internal hemorrhage any organ may be involved. If necessary, a transverse incision may be added. If there are tears extending deep into the parenchyma the spleen should be removed. In superficial tears of the capsule it should be tamponed, as suture is always uncertain.

In all of his cases the writer collected the **blood** from the abdominal cavity, **mixed** it **with** 0.5 per cent. **sodium citrate solution,** and **reinjected** it intravenously. He thinks he thereby saved many lives. H. Hauke (Beitr. z. klin. Chir., cxxii, 389, 1921).

Kidneys.—Symptoms frequently accompanying wounds of the abdominal organs—extreme pallor, weak pulse, cold extremities, nausea, and vomiting—are apt to be most marked when, besides the organ itself, the peritoneum has been pierced.

A wound of the kidney gives rise to severe pain in the majority of cases, but this symptom may be absent. As in cases of laceration, the pain radiates in various directions, especially in the direction of the external genital organs. The testicle of the corresponding side, besides being the seat of considerable suffering, is frequently raised by spasmodic contractions of the scrotum.

At first a small quantity of bloody urine may be passed, but this is often followed by vesical tenesmus and complete retention, due to the presence of clots in the bladder.

Much information is sometimes obtained by a close examination of the wound of exit. If the track of the bullet be anteroposterior and the missile have entered from the front and penetrated the kidney, the exit wound will be found in the lumbar region. It is frequently found in this situation to contain urine, a positive indication that the organ or its annex, the ureter, has been wounded.

In injuries of the kidneys, simple perforations are often negligible. Hematuria, rarely severe or persistent, was observed in only 11 out of 27 cases. Its degree in no way accords with the severity of renal damage. External escape of urine was noted in only 7 cases. In 17 fatal cases, 7 were due to secondary hemorrhage, which occurred in 12 instances, usually about the fourteenth day. In every case of secondary hemorrhage the urine was infected. The hemorrhage occurred either as a persistent hematuria or a perirenal hematoma travelling into the iliac fossa and along Poupart's ligament, with skin ecchymoses and slight fever. Makins (Brit. Jour. Surg., iii, 645, 1916).

Cystoscopy was employed in a number of cases to determine loss of renal function and in latent cases, the presence of bladder injury. The X-rays were used to advantage to determine the presence of and locate accurately missile fragments. The complications seen included sepsis, secondary hemorrhage, and urinary fistula. The last occurs when there is a wound of the pelvis, or the tear in the parenchyma extends into the pelvis, or when the ureter is torn. The chief causes of death were sepsis and secondary hemorrhage. Of 42 cases studied, 5 died. A. Fullerton (Brit. Jour. of Surg., Oct., 1917).

The conditions which make an isolated kidney wound dangerous are hemorrhage and infection. In 46 fresh kidney wounds severe hemorrhage was observed in 6. In 3 of these cases where there was a concomitant liver wound, the patients died. In 3 of the cases the hemorrhage was a hematuria; 2 died within a few hours. In 5 cases a perirenal hematoma was produced. Of 35 remaining patients who showed no special symptoms necessitating immediate action, a primary operation was done in 11 cases, a secondary operation in 2, and abstention was observed in 22. The primary operation consisted either in a nephrectomy or in cleansing and drainage of the trajectory. Of 3 nephrectomized cases, 2 died; of 4 tamponed patients, 3 died; 1 hematoma drained recovered; 5 clearance and drainage operations recovered; 22 abstentions from surgical intervention gave 3 deaths and 19 recoveries. M. Chevassu (Bull. et mém. Soc. de chir. de Paris, xliv, 81, 1918).

If the wound of entrance be in the back, its location over the site of the kidney may suggest a lesion of the latter; but the urine test will only be of value if the projectile only penetrate the kidney without perforating it.

If it penetrate the organ, the extravasation will take place into the peritoneal cavity. The same will be the case if the missile enter from the front without going through the organ. Bullets buried in the renal parenchyma either become encysted or cause abscesses, and pass out through the ureters or into the adjoining parts.

Bladder.—The symptoms vary according to the location of the wound. A perforation between the symphysis and the peritoneum above does not give rise to general symptoms; whereas shock, pallor, weak pulse, vomiting, etc., may be much marked when the peritoneum is involved in the injury. In all cases, however, severe pain is experienced at the site

of the lesion and radiating to the thighs and testicles.

The passage of urine soon becomes very difficult and spasmodic. It may be voided, drop by drop, for a long while, notwithstanding the efforts of the patient, then suddenly gush out for a few moments and again flow slowly. This symptom may be due to accumulation of clots or to spasm of the urethra. If the catheter is passed, hematuria becomes evident when the bladder has been penetrated: a characteristic sign.

As in the case of rupture due to contusion, infiltration may take place through the wound into the neighboring tissues; any obstacle to the free passage of urine greatly encourages this. Hence the necessity, in all bladder lesions, of keeping the organ as free as possible by the frequent use of the catheter.

The writer in a study of 53 cases calls attention to the comparative rarity of injuries of the bladder in warfare, the percentage of total wounds reaching the base being not more than 1 in 3000 or 4000. The bladder in a collapsed state occupies so little space that it forms a very small target for the missiles of war. Just before an attack the nervous tension presupposes an evacuation of the bladder contents. If the patient is caught unawares at other times, the organ may be in a state of distention. The prostate because of its proximity to the neck of the bladder is frequently injured with it.

In the 53 cases reported, the injury to the bladder was caused by bayonet in 2 cases; by shell in 24 cases; by bullets (rifle or machinegun) in 12; in 7 by shrapnel; in 1 case indirectly by a shell and directly by a fall of earth on the abdomen; in 7 cases the nature of the missile was unknown. In nearly 75 per cent., therefore, there was a wound in the buttock region reaching as far as, or actually penetrating, the bladder. The suprapubic route was comparatively rare.

The foreign body was retained in 33 cases. In 10 it came to rest in the bladder. In the remaining cases it lodged in the pelvis or its walls, occasionally between the bladder and rectum. The entrance wound is frequently of small size and comparatively insignificant on superficial examination. The wound in the bladder itself was of the most varied nature, a perforation, tear or slit, and in 1 case a considerable portion of the bladder wall had been shot away.

The gravity of bladder injuries is greatly enhanced by associated damage to adjacent structures such as intestine or bone. Shock is likely to be present when other severe injuries complicate the case. According to Wallace, it is one of the chief causes of death at the clearing stations.

Hemorrhage also contributes largely to the high mortality of such wounds. Leakage of urine is one of the most important complications. This may appear at the wound in the parietes, or be more or less concealed in the form of extravasation into cellular tissue or leakage into the peritoneal cavity. In cases reaching the base, a urinary fistula was most frequent in the region of the buttock.

A sudden, sharp pain may occur when the bladder is struck, but when the patient reaches the base, this pain is not a constant feature. There is some tenderness and rigidity in the hypogastrium in a fair proportion of the cases. Vomiting is occasionally seen in cases in which the peritoneal coat is intact. On the other hand, it may be entirely absent in the first hours of an intraperitoneal lesion. As in most war wounds, fever is commonly present, and depends largely upon the amount of infection in the soft parts and bone.

The mortality in bladder wounds is rather high. Wallace states that in uncomplicated cases it is 56 per cent.,

and in complicated cases the picture is dismal in the extreme. In the writer's series of 53 cases, the mortality was over 24 per cent. A. Fullerton (Brit. Med. Jour., vi, 24, 1918).

PROGNOSIS.—Gunshot wounds are more fatal than stab wounds, but stab wounds, in which the peritoneum is penetrated, are fully as fatal as gunshot wounds.

The kind of weapon inflicting the injury plays an important rôle in this connection. A triple-edged bayonet is more likely to produce a serious laceration than a flat blade. Again, wounds caused by small weapons, such as a Flobert rifle, for instance, would hardly produce lesions to be compared to the old Enfield or Minie rifles, which sometimes caused a large portion of an organ to protrude through a wound of exit the size of an apple.

> Report of 44 cases of penetrating abdominal wounds, all in civil practice. Of 6 cases without laparotomy 4 died. Among 38 penetrating wounds the mortality was 45 per cent.; among 31 penetrating wounds of hollow viscera, 51.5 per cent.; among 25 gunshot wounds of hollow viscera, 60 per cent., and among 6 stab wounds perforating hollow viscera, 16.3 per cent. Of 7 cases of injuries of the liver, spleen, and other structures, with no involvement of hollow organs, 6 recovered. Stomach perforation occurred in 11 cases, with 5 recoveries, and intestinal perforations in 29 cases, with 15 recoveries. Randolph Winslow (Jour. Amer. Med. Assoc., Oct. 3, 1914).

Portions of the solid viscera are sometimes cut off or shot off, leaving a gaping tear, which greatly compromises the issue. Again, as is often the case with the liver, the bullet, or any foreign material dragged in by the latter, may lead to

complications which greatly reduce the chances of recovery.

An important factor is the time elapsing between the receipt of the injury and that at which competent treatment is applied in mild cases. This is especially true as regards the early utilization of surgical measures when these become necessary. The sooner these are instituted, the more favorable the prognosis, especially during the first ten hours.

The relation between spontaneous cures and operative interference as worked out by Eisendrath is about as follows:—

SPONTANEOUS RECOVERIES.

	PER CENT.
Spleen	15.8
Liver	21.8
Intestines	7.
Kidney (extraperitoneal)	70.
Kidney (intraperitoneal)	0.
Bladder (intraperitoneal)	2.
Bladder (extraperitoneal)	11.

OPERATIVE RECOVERIES.

PER CENT.

56.   (50 cases).
59.5 (37 cases).
48.   (42 cases prior to 1896).
50.   (38 cases since 1896).
80.
100. (6 cases).
52.   (43 cases).
30.   (last 15 years).—Mitchell.

In 1917, Rouvillois and his associates presented the following figures concerning abdominal war wound cases treated in a French automobile surgical ambulance :—

RECOVERIES.

	PER CENT.
Small intestine (39 cases)	28.3
Cecocolon (17 cases)	41.2
Liver (7 cases)	28.6
Stomach (6 cases)	66.7
Spleen (2 cases)	50.0

> Hemorrhage is a great enemy of the wounded subject in abdominal wounds, owing to the fact that there

is little tendency toward spontaneous arrest. Three or four hours after an injury small arteries in wounded bowel are still spurting vigorously. Hence the necessity and value of rapid transportation of these sufferers to a suitably equipped operating room. H. H. Sampson (Brit. Med. Jour., Apr. 11, 1916).

Much bleeding occurs from injured gastric vessels, omentum, mesentery, retroperitoneal tissue, abdominal wall (deep epigastric artery), pelvic veins, liver, kidney, and spleen. The intestinal walls, on the other hand, do not bleed to any appreciable amount. Pallor and pulse are the best criteria as to the blood lost. If near a wound in the bowel, bleeding may aggravate the situation by carrying infection to distant parts of the abdomen. Retroperitoneal infection may occur with or without a wound of the bowel; where the bowel is injured, the colon is usually the part implicated, the entrance wound being on the flank or loin. From retroperitoneal gas infection the peritoneum may be pushed forward as in retroperitoneal hemorrhage; such cases are nearly always fatal. The operation site, too, becomes badly infected in many instances of penetrating abdominal wound, the origin of acute infection being in the peritoneal cavity. Virulent wound sepsis may occur even after a lesion of the small bowel has been successfully dealt with by the surgeon. Death from peritonitis in abdominal wounds usually occurs on the third to fifth day, but may occur within 24 hours or in 10 days. The degree of bowel distention is a better prognostic guide than the amount of exudate present. Wallace (Pract., Sept., 1916).

In abdominal wounds the mortality, excluding moribund cases, was 50 per cent. The total operative mortality was 54 per cent. That of hollow viscera, 65 per cent.; of stomach, 53 per cent.; of small intestine, 66 per cent.; and of great intestine, 59 per cent.

Among 263 abdominal wounds at an advance station, the patients operated on between 1 to 6 hours after wounding were 43; recovered, 27, or 62.8 per cent.; died, 16, or 37.2 per cent. Cases operated 6 to 12 hours after wounding, 33; recovered, 12, or 36.3 per cent.; died, 21, or 63.7 per cent. Patients operated on between 12 to 16 hours after wounding, 18; recovered, 3, or 16.6 per cent.; died, 15, or 83.4 per cent. Patients operated on over 24 hours after being wounded, 11; recovered, 5, or 45.4 per cent.; died, 6, or 54.6 per cent.; recoveries at 48, 36, 33½, 32 and 30 hours, respectively. Wallace (Lancet, Apr. 28, 1917).

Report on 263 cases of abdominal wounds encountered at a hospital stationed close up to the fighting line and thoroughly equipped for dealing with urgent surgical work. Recovered, 136, 51 per cent. Died, 127, 49 per cent. Number admitted "with penetration," 180. Number on whom a laparotomy was performed, 110. Recovered, 46, 41.5 per cent. Died, 64, 58.5 per cent. Hughes and Rees (Lancet, Apr. 28, 1917).

Of the patients who survive operation performed in the first twelve hours a high proportion will have had their lives saved by it, and this is true in a lesser degree of those operated on in the second twelve hours. After this time most of those who survive operation are those whose injuries were not originally fatal. Owen Richards (Brit. Med. Jour., Apr. 27, 1918).

Report of the case of a man in whom a steel rod one-half inch in diameter and 54 feet long, in falling, entered the body just behind the left shoulder and emerged at the inner aspect of the right knee. After passing through the posterior aspect of the left lung, the rod penetrated obliquely through the bodies of 3 or 4 vertebræ in the lower dorsal and upper lumbar regions. Below this it could be felt below the pole of the right kidney and just behind the inferior vena cava. At this point it passed for about one-half inch into

the peritoneal cavity without causing any damage, and again became extra-peritoneal by penetrating the psoas muscle. It appeared to leave the abdominal cavity by drilling a hole through the brim of the pelvis behind the acetabulum. Recovery from the shock was rapid. The upper end of the rod having been sterilized, traction was applied in the direction of the curvature of the rod, which was thus slowly removed while a close watch was kept for internal hemor rhage, etc. The resulting shock was great but yielded to treatment. Uneventful recovery followed. Lake (Lancet, Apr. 23, 1921).

Intestines.—The prognosis depends greatly upon the nature of the lesions. Stab wounds opening the intestine lengthwise, if small, often heal of their own accord; transverse wounds are more serious, while complete section of the bowel is a very dangerous complication. Gunshot wounds show a great fatality. Prior to the introduction of antiseptic surgery the mortality exceeded 90 per cent.; since then, the mortality has been reduced to 40 per cent. or less in cases operated during the first twelve hours. Perforated wounds of the descending colon and sigmoid flexure are seldom fatal; those of the transverse colon give a worse prognosis, by the formation of fistulæ, adhesions, and abnormal communications. Again, diatheses may compromise recovery.

The authors noticed that the less the damage to the gut—when the lumen had been entered—the greater the likelihood of extensive peritoneal soiling; this is ascribed to the inhibition of peristalsis in massive injuries, which is incomplete or absent in the lesser ones. Fraser and Bates (Brit. Med. Jour., Apr. 8, 1916).

Infection of the small and large bowel exhibit a radical difference in that, whereas the former tend to spread progressively, the latter if undisturbed, tend to become localized. As regards the small intestine, there does not seem to be much danger of infection in the first few hours, but a critical period would appear to be at the eighth to the twelfth hour. The infection does not usually result from extrusion of the bowel contents, for the viscus is generally empty and paralyzed, but probably from the carrying out of infection by the projectile and the everted mucous membrane. For some hours the coils stay in the position in which they were when wounded. At a later period they are found, on the contrary, thin and distended, due to beginning infection. Small gut injuries, as a whole, are serious from their multiplicity. The lesions vary from a small perforation to complete division or destruction of a part of the bowel. Bomb wounds, small though often multiple, are favorable, usually lending themselves well to suture. Bullets cause all sorts of injuries, often as severe as those due to larger shell fragments. Wallace (Pract., Sept., 1916).

Septic infiltration of retroperitoneal tissue seems a frequent lethal factor in large gut wounds. Wounds of the transverse colon are more apt to be multiple than those of the other divisions of this gut. Wounds of the rectum are divided into those complicating wounds of the buttocks, ischial fossæ, or perineum, and those caused by missiles entering the lower abdomen. With the former the greatest danger is septic absorption, but, on the whole, extensive buttock wounds do not do badly at the front, being widely open from the nature of the injury.

With the abdominal type, severe multiple injury of the small bowel, and also injury of the bladder, are likely to accompany the rectal wound. Septic peritonitis is to be feared. Wallace (Lancet, Mar. 4, 1916).

Stomach.—Uncomplicated wounds of this organ frequently yield without

trouble when the bullet, blade, or other instrument causing the perforation is small, especially if the stomach was empty at the time the injury was inflicted. The mucous membrane bulges out and forms a plug which obturates the hole until reparative processes have sealed the aperture on the peritoneal side. Complicated cases, in which the lesions are extensive, soon reach a fatal issue if deprived of timely surgical intervention.

Many cases of injury limited to the stomach have died, after successful suture, from the effects of primary gastric hemorrhage. The escape of food from the wounded stomach depends not only on the time of the last meal, but also on the size and situation of the wound. If the wound is small and near the lesser curvature or cardiac end, little food escapes, while if it is large and near the greater curvature, marked extravasation may occur.

Liver.—The prognosis of wounds of the liver depends mainly upon the complications. If the patient does not die from hemorrhage soon after the receipt of the injury, he is still exposed to the results of extravasation into the peritoneal cavity, the presence in the liver of a foreign body,—the bullet and what material it may have forced into the wounds, —etc. Peritonitis, hepatitis, and abscess are, therefore, dangers to be taken into consideration. Hepatitis and abscess are much less to be feared, however, from stab wounds, no foreign body being left behind, unless, as in dueling, the sword-point strike the spinal column, causing the blade to break. In such an event, however, the hemorrhage would probably prove mortal very rapidly.

As to mortality, the statistics of Edler, Mayer, and others show it to average about 50 per cent., including the cases attended by complications.

> The most extensive injuries to the liver are frequently not incompatible with life. One patient who recovered lost a transverse section of the entire upper abdominal wall some 3 inches in width, with a groove in the liver substance which almost bisected it. The lower half of the liver was stitched into the defect in the abdominal wall. R. E. Skeel (N. Y. Med. Jour., Oct. 18, 1919).

Spleen.—Slight punctured wounds of the spleen are not mortal unless complicated with laceration of a large artery. They are sometimes followed by abscesses which heal after a prolonged period in the great majority of cases. Severe punctured wounds are dangerous in proportion, but, if the primary hemorrhage is not such as to cause an early fatal issue, the chances of recovery are about those of slight wounds.

Gunshot wounds are much more serious as a result of rupture of the spleen taking place under the concussion. When the bullet is large and its velocity is great, fatal hemorrhage quickly ensues. Rupture of the spleen may also occur during convalescence.

During the War of the Rebellion the proportion of deaths was 93 per cent. In civil life, however, the weapons used are, as a rule, less powerful, and the mortality is much smaller. In the European war a mortality as low as 37.5 per cent. in 8 cases was reported by Duval. The predilection of this organ for abscess tends to compromise recovery.

Kidneys.—Complications are also to be feared in lesions of this organ,

namely: peritonitis, nephritis, and secondary hemorrhage. Again, the position of the kidney makes it probable that other organs are also injured in the majority of cases. The direction from which the bullet or stab came, the length of the penetrating blade, etc., are important factors when the nature of the injury is to be determined.

Bladder.—Gunshot wounds of the bladder are always serious as far as complications are concerned, rectal, vaginal, perineal, and scrotal fistulæ being very frequent.

As to the mortality of penetrating wounds of the bladder, it is not so great as in lesions of any of the other abdominal organs. Stab wounds are more frequently mortal than uncomplicated bullet wounds, the proportions being 29 per cent. in the former and 17 per cent. in the latter. When, however, osseous lesions are also present, penetration or fracture of the pelvis, etc., the mortality reaches 29 per cent.

TREATMENT.—The preliminary measures indicated in the treatment of complicated contusions of the abdomen are also applicable in that of penetrating wounds of that cavity. Protrusion of portions of the intestines, the mesentery, and the omentum through the external wound is an early complication met with in many cases of penetrating wound. If the protruding mass be intestinal and in good condition it should at once be returned into the abdomen. An easy way of accomplishing this (recommended by Levis) is to raise the middle of the patient's body by means of a pillow, the hands, etc., while he is lying on his back. The anterior portion of the pelvis is thus separated

to an abnormal degree from the anterior portion of the thorax, and the increased room in the abdominal cavity thus obtained causes the intestines to spread out, as it were, and, their weight causing traction upon the protruding loop, the latter quickly slips in.

At times the accumulation of gas or fecal matter checks its inward progress; the gas can easily be let out by inserting a clean hypodermic needle into the projecting bowel; the fecal matter can also be reduced in quantity by drawing out an additional portion of the gut—thus increasing the size of the loop—and gently pressing small portions of the contents into the unprolapsed bowel, thus diminishing the tension of the protruded mass. It is sometimes necessary to enlarge the abdominal wound. If the projecting mass be greatly inflamed the latter procedure is unavoidable. If it be gangrenous it had better be incised and the formation of a fecal fistula permitted.

An omental protrusion, if healthy, can be immediately returned, but if greatly inflamed or gangrenous it should be transfixed near the abdominal wall and tied with a double ligature; then excised. The stump is then secured in the deeper portion of the wound with ligatures and adhesive strips.

Punctured wounds of the abdomen are frequently recovered from spontaneously, owing to the absence of serious visceral lesions. The same statement may be made as regards bullet wounds, but with less emphasis.

Of serious abdominal injuries 20 per cent. are hopeless, and of the remaining 80 per cent., not less than

60 per cent. should recover after early operation under proper conditions. Rutherford Morison (Oxford War Primers, 1915).

Surgeons are agreed that wounds of the small gut area should be explored. There is still some doubt, however, about cases of suspected stomach injury and of wounds apparently involving the colon. Wounds limited to the liver furnish most of the cases of undoubted penetration which it is advisable to leave alone; the kidney and spleen furnish a few of these. While hemorrhage is itself a sufficient reason for operation, especially if the case is seen early and the bleeding presumably continuing, the many cases presenting a single entry of a missile, particularly in the back, buttocks, thighs, and lower thorax, without signs of bleeding, are perplexing to the surgeon. If the latter does not feel justified in operating on principle, he must watch the pulse and the abdominal rigidity.

As a rule, within 4 or 5 hours the abdomen will harden or the pulse rise above 100, or both, if the intestine has been wounded, thus indicating operation. In lower thoracic wounds the abdominal rigidity must be discounted, but in suspicious thigh and buttock wounds, rigidity and rapid rising pulse are urgent signals for operation. Single wounds of the posterior aspect of the flanks present many difficulties. Since a median incision to explore the small bowel in such cases may lead to dissemination of a previously local infection about the colon, possibly the best course is a local exploration through a transverse loin incision, or a careful watch for abdominal involvement. With regard to stomach wounds, Wallace favors routine operation on account of the danger attending hemorrhage from vessels supplying this organ. Withholding operation, the favorable moment for dealing with this hemorrhage may be passed before the signs of anemia appear; or, there may be associated lesions of other organs that will prove fatal.

Cuthbert Wallace (Pract., Sept., 1916).

Report on 56 non-military cases of stab and gunshot wounds of the abdomen, mostly revolver wounds. Severe lacerations of internal organs, such as are observed in war wounds, were not found. There were 35 perforating wounds with injuries to internal organs, with 8 deaths, and 10 perforating wounds without injury to internal organs and 11 non-perforating wounds without any deaths.

Immediate, careful transport of the patient should follow the application of a **compression bandage**. Every wound of the abdominal wall should be widened as early as possible in order that it may be determined whether the peritoneum is involved. If so, **laparotomy** is indicated.

The positive indications for operative treatment are: (1) Extrusion of abdominal organs; (2) escape of gastro-intestinal contents or urine from the external wounds; (3) severe anemia, with an increasing zone of dullness indicating severe hemorrhage; (4) X-ray demonstrations of the escape of gas into the peritoneal cavity. W. Smital (Wien. med. Woch., lxx, 653, 1257, 1305, 1442, 1501, 1547, 1601, 1920).

When surgical measures become necessary, including enlargement of the wound, the patient should be placed under an anesthetic. The rectum should be emptied by copious injections containing a tablespoonful of **glycerin** to the pint. A subcutaneous injection of **morphine** ($\frac{1}{4}$ grain) is generally recommended. **Rectal injection of whisky and warm water,** 2 ounces of the former and 4 of the latter, is useful to sustain cardiac action. It may be repeated in an hour if evidences of impending shock are still present. In patients with nervous shock or severe hemorrhage, **camphorated oil, ether,** and **saline** injections with $\frac{1}{60}$ grain (0.001

Gm.) of **adrenalin** have proven useful. **Intravenous saline infusion** may be continued during the operation.

It is deemed necessary to get the patient thoroughly warm before operation, and to minimize shock in every way, the room being well heated and the table provided with a **hot water bed.** The writers advise operating these cases in the **Trendelenburg position.** Just before beginning, **subcutaneous saline** administration is started, and this is continued throughout the operation, 3 or 4 pints of fluid being thus given. Henderson's **closed ether anesthesia** is preferred. Fraser and Bates (Brit. Med. Jour., Apr. 8, 1916).

A pulseless patient never benefits by operation. A total absence of pulse, however, must not be confounded with an extremely rapid pulse, which perhaps cannot be counted. Such patients may be snatched from death by operation. A truly pulseless patient must be treated first and every effort made to bring back the arterial tension; while with a patient who still has a pulse no time should be lost in ligating large blood-vessels and removing possible causes of sepsis. Operation within three hours has shown a superiority over longer periods. Patients with very little traumatic shock and otherwise in good condition are practically certain to recover after very early intervention. Vaquez has shown that after ordinary laparotomy, a blood-pressure of 140 may be lowered to 100. Operation on a patient with a tension below 100 is inevitably followed by death inside of twelve hours. Below 100, the lower the tension the worse the outlook. It should be 120 and upward before one can feel certain of recovery. Quenu (Bull. Méd., Oct. 28, 1916).

The efficient treatment of gunshot wounds involves the 2 principles of antisepsis and osmosis. These 2 principles, according to the writer, are fulfilled by a combination of equal parts of **ichthyol** and **glycerin** which

he has been using in various military and civil hospitals for nearly 3 years. It is particularly efficient in wounds that refuse to heal under classic measures. Duggan (Pract. June, 1918).

If, after a careful examination of the enlarged wound, it is found that the peritoneum is not involved, the exposed tissues are carefully cleansed and the wound is closed, deep sutures being used to hold the tissues in accurate apposition. As already stated, the possibility of ventral hernia should be borne in mind: the patient should be kept in bed for some time and a bandage be worn until all local weakness has disappeared.

If the lesion is intraperitoneal, a median incision of good size should always be used.

The presence of gas indicates a lesion of the intestinal canal, requiring examination of the whole canal, with closure of each hole as it is reached.

All drains should be removed at the end of 36 to 48 hours. The wounds should be closed with through and through **sutures** of silkworm gut, as closure can thus be more rapidly done. The patient should be placed in the **Fowler position** and **proctoclysis** immediately instituted. **Morphine** and **atropine** are prescribed as required. If undue vomiting occurs the **stomach** should be **washed out.** No attempt to move the bowels should be made for 3 or 4 days. F. W. McGuire (N. Y. Med. Jour., Sept. 21, 1921).

If, after a stab wound, the parietal peritoneum alone is found incised or penetrated and there is no evidence that the organs behind have suffered injury, the tissues must be cleansed with great care and the peritoneal flaps brought together, the serous surfaces being kept in contact. A continuous catgut suture is used for the peritoneum; the muscles and skin

are then united and the wound is closed. The measures already outlined to prevent ventral hernia are also indicated for the deeper wound.

When laparotomy becomes necessary the incision should be made in a spot affording the operator the greatest opportunity for a wide field of action, and should be sufficiently long. When performed for the arrest of dangerous hemorrhage, a long median incision will enable the surgeon to reach any organ with ease: an important factor, for the missile or blade inflicting the injury may have traversed harmlessly between several coils of intestine and have caused a rent in the organ most remote from the point of entrance. Again, the incision should be free, so as to make it possible to easily reach all parts of the abdomen to allow of a thorough removal of all extravasations which might otherwise ultimately cause complications.

As the late Nicholas Senn taught, one of the important elements of success in the treatment of gunshot and stab wounds of the stomach is time. Unnecessary time lost in finding and suturing the visceral wounds is a source of immediate danger to life which should be eliminated as far as possible by means which enable the surgeon to make a quick and correct diagnosis, and by resorting to a method of suturing which closes the wound safely and securely with the least possible delay, and which leaves it in a condition most favorable for speedy definite healing. It is well known that small penetrating wounds of the stomach often heal without operative intervention. By contraction and relative displacement of the different muscular layers of the thick

wall of the stomach the tubular wound is contracted and obstructed sufficiently to prevent leakage until the canal on the peritoneal side becomes hermetically sealed by firm plastic adhesions which prevent extravasation during the time required for the repair of the visceral wound. If in larger wounds of the stomach the same degree of occlusion can be accomplished by the simplest mechanical means, then such a procedure should take the place of the more time-consuming methods of suturing now in general use. This can be accomplished with the purse-string suture.

In gunshot injuries the defect in the stomach-wall is circular and the wound-margins contused; hence the deep sutures could at first furnish a barrier to the escape of stomach-contents only for a short time, as their hold in the necrosed tissues would be imperfect and only of brief duration. In short round wounds the circular suture is the one which will bring and hold together in permanent uninterrupted contact the serous surfaces in the most efficient manner. In the treatment of gunshot wounds of the stomach the principal object of suturing should be to close the perforation in such a way as to guard securely against extravasation, and at the same time approximate and hold in apposition a maximum surface by intact healthy peritoneum. This is accomplished by making a cone of the injured part of the stomach with the apex corresponding with the wound directed toward the lumen of the organ. The purse-string suture applied in the manner that will be described in the experimental part of this section will maintain this cone

until the healing of the visceral wound has advanced sufficiently to render further mechanical support superfluous. The cone on the mucous side of the stomach acts in the manner of a valve, which in itself is an effective barrier against the escape of stomach-contents, while the circular suture constitutes almost an absolute safeguard against leakage, and brings in contact the serous surfaces in the interior of the cone. For wounds of the posterior wall of the stomach the author recommends a purse-string suture of heavy durable catgut to be applied through the anterior wound. The anterior wound is closed with a purse-string suture of silk of medium size applied to the base of the cone on the serous side. It is desirable that the circular suture should cause no necrosis of the included tissues. By using an absorbable suture in closing the posterior wound in the interior of the stomach this object is gained, as only a small part of the thickness of the stomach-wall is subjected to pressure, and the tension caused by the ligature is gradually lessened by softening of its material, and is entirely removed by the absorption and digestion of the ligature in less than three weeks.

The wound of the posterior wall of the stomach is found and made accessible by inserting through the anterior wound a grasping forceps with which the posterior wall is seized at a point where, from the course of the bullet, the second wound is supposed to be located. Through a wound large enough to admit the index finger the greater part of the posterior wall of the stomach can be made accessible to sight and touch, and the perforation can be located and closed with the purse-string suture in a few moments. In doubtful cases inflation of the stomach should invariably be practised for the detection of a second and possibly a third perforation.

The experiments demonstrated the safety of the circular suture in the treatment of gunshot and other penetrating wounds of the stomach. All of the animals operated upon in this manner recovered and the repair of the injuries as shown by the specimens are ideal. The absence of adhesions over the posterior wound and their constant presence over the anterior wound indicate that the presence of the silk ligature and the needle punctures were the causes of the circumscribed plastic peritonitis which produced them. In none of the specimens could any indications be found of necrosis of any of the inverted tissues, and included in part by the circular suture.

In the course of three weeks the continuity of the mucosa at the seat of the injury was completely restored. The result of these experiences has convinced the author that the circular suture compares favorably with the methods of suturing in general use, and besides has the great advantages over them in the case of its application and the saving of much valuable time.

Suturing of the posterior wound by partial eversion of the stomach through the anterior obviates unnecessary handling of the organ and the necessity of interfering with the vascular supply incident to exposure of the posterior wound, as is done by the methods most generally practised. If extravasation into the retrogastric space has taken place, flushing through the posterior wound and a

vertical slit in the gastrocolic ligament and gauze drainage through the latter are invariably indicated.

The stomach and the transverse colon are best brought to view by an incision through the rectus muscle. In the case of the stomach hernia of the mucous membrane will facilitate recognition of the lesion. The ascending colon requires lateral incision on the right side, and the descending on the left. These also should be sufficiently long to facilitate the search for the injury or injuries that may be present in the organ itself and beyond.

> In cases seen later, when peritonitis has already set in, a small suprapubic incision for insertion of a tube to the bottom of the pelvis, with the Fowler position, will give the patient a chance of recovery. Mayo-Robson (Brit. Med. Jour., Dec. 4, 1915).

The incision may be such as to intersect the wound of entrance. This is desirable at all times, the aim being, of course, to always avoid unnecessary solutions of continuity. Such an incision can fortunately be made in many of the cases in which the hemorrhage is not formidable.

> In abdominal cases where there is much blood, the authors quickly swab it away with a long roll of dry gauze before examining the viscera. In early cases with extensive peritoneal soiling they wash out the peritoneal cavity; in later cases, and those with signs of peritonitis, they do not. Drainage by a single Keith's tube passing into the pouch of Douglas proves sufficient; in special instances local or flank drainage is necessary. Fraser and Bates (Brit. Med. Jour., Apr. 8, 1916).

> Experience in 356 cases showed that for injuries of the small intestines either pursestring suture or resection should be employed, the former being given preference wherever

possible. When resection is required end-to-end anastomosis seems to give better results than lateral and is more rapid. Extravasated material is best removed by mopping with gauze wrung out of hot saline. Saline should never be used for lavage of the abdominal cavity. Lockwood, Kennedy, Macfie and Charles (Brit. Med. Jour., Mar. 10, 1917).

> No important change in the technique of operation in gunshot wounds of the abdomen was introduced during the war, except that it became the rule to close without drainage. A drain often leads to infection. Frequently all layers of the abdominal wall were closed but the skin, as late infections often resulted from the latter. If a drain is used at all, it should be a loose gauze drain. The mortality in gunshot abdominal wounds was extremely high; but this mortality occurred largely on the field as a result of hemorrhage and shock. J. H. Gibbon (N. Y. Med. Jour., June 28, 1919).

Hemorrhage.—When the abdominal cavity is opened and the hemorrhage, which is usually more venous than arterial, is marked, the blood rapidly accumulates in the most depressed portion of the cavity from an invisible source. To mop out the blood with sponges is generally recommended; but such a procedure does not cause the hemorrhage to cease,—the first *desideratum*. In these formidable cases an assistant should at once introduce his hand through the wound—hence the advisability of a long incision—and compress the abdominal aorta below the diaphragm. This procedure immediately checks the flow.

If any difficulty is experienced, the digital pressure upon the aorta may, for an instant, be decreased, and a sudden gush will point to at least the direction from which the blood comes.

The necessary steps are then taken to arrest the flow, and the abdominal aorta is released as soon as possible, —not suddenly, but by a gradual reduction of pressure.

The measures to be employed in arresting hemorrhage vary according to the organ involved. Gunshot wounds of the liver are frequently stellate, and rents, radiating from the bullet-track in various directions, greatly increase the bleeding surface, the parenchyma in this organ taking part to a great degree in the emission of blood. To force resilient sponges into these tears is to increase their depth. If the wound be not very extensive, it may be sutured with catgut or cauterized with the actual cautery. If the wound is extensive it had better be packed with long strips of iodoform gauze, one end of which is brought out of the external wound.

Of 5 cases in which projectiles were extracted from the liver. In only 1 was the projectile removed immediately after the injury. In the other four it had remained in the liver for from 10 to 23 months.

In all cases the extraction was done under the control of the radioscopic screen.

In but 1 instance was the operation indicated by the symptoms of secondary infection; in the others the indication was furnished by the pain caused by the projectile. In 1 case the extraction was done by the lumbar route; in the others, by laparotomy.

The incision in the liver varied from 1 to 3 cm. in length according to the size of the projectile. The projectile was removed with the forceps. In no case was there any extensive hemorrhage, but in 1 instance a pyopneumothorax developed, following the operation. L. Sauvé (Bull. et mém. de la Soc. de Chir. de Paris, xlv, 1461, 1919).

The spleen is next in order as to profuseness of hemorrhage. The same procedures may be adopted as for the liver, but the introduction of iodoform strips is to be preferred. If these means fail, splenectomy is the only measure left.

Sometimes a portion of the organ projects through the wound; removal of the protruding portion should be practised after passing a ligature around the mass.

The walls of the stomach and intestines may also give rise to marked hemorrhage notwithstanding their comparative thinness. The number of vessels coursing through them, however, is very great. In these cases it is best to hem the margins of the wounds with fine silk. The bladder may be treated in the same way.

The mesentery sometimes bleeds profusely when perforated. The mesenteric vessels should be ligated *en masse* with fine silk.

Blood escaping through bullet holes in the bowel gradually works its way downward into the small pelvis and is not absorbed. Often an abscess forms, and later walling-off adhesions are broken down and secondary peritonitis results, usually extremely serious. There are two ways to render harmless the infected extravasated blood: (1) When the patient is seen in the first twenty-four or forty-eight hours a very small laparotomy incision is made above the symphysis (under local anesthesia) just large enough for a rubber drain the size of the finger, to be carried down into the small pelvis. The patient keeps in a half-sitting position or lies on his side. (2) When not seen until later, the space between the rectum and the bladder must be carefully examined through the rectum. If there is any tenderness, protrusion, tenesmus or

difficulty in micturition, the region is opened up at once. Payr (Münch. med. Woch., Aug. 18, 1914).

Report of the case of a man who had received 2 stab wounds, 1 through the costal cartilage of the left side and 1 in the right thigh. At operation the peritoneal cavity was found full of blood, and an incised wound on the stomach was bleeding. This was closed by a double row of **Lembert sutures.** Shock, secondary anemia, and collapse followed, and the patient continued to vomit blood, also developed evidences of pneumonia. **Bayliss's gum acacia solution** and **blood transfusion,** however, turned the tide, and he ultimately recovered. C. W. Bowle (Jour. Royal Army Med. Corps, Apr., 1921)

Hemorrhage of the kidney is arrested in the majority of cases by iodoform-gauze package. If this should prove ineffectual the organ must be exposed and the vessels tied if possible. If not, nephrotomy or nephrectomy should be resorted to. The latter operation does away with the chances of complication attending the former, while the kidney of the other side assumes the function of both.

For extraperitoneal injuries of the anterior aspect of the bladder, if high and if after regularization they can be correctly sutured, the practice should be suture with a permanent catheter. If the lesion is in the vicinity of the neck, suture should not be tried. The practice should be cystostomy as high as possible and a catheter placed after an interval. For intraperitoneal injuries, if in the apex or the posterior aspect, resection of the margins is indicated, suturing in two places with fine catgut, and a permanent catheter. The Douglas sac should be closed by a row of sutures, thus isolating the wound from the rest of the abdominal cavity, to be followed by cystostomy. As wounds of the fundus are usually produced by perineal projectiles, they necessitate a lateral perineotomy or even a transverse, made as wide as possible so that a loose tamponade in contact with the bladder wall may be instituted. H. Brin (Bull. et mem. Soc. de Chir. de Paris, xliii, 1086, 1917).

Of 43 bladder wounds met with since the beginning of the war, 6 ran a benign course. Such are usually bullet wounds; shell wounds show marked tears and easily produce a septic condition. In 15 cases there was a vesico-intestinal fistula, with 12 spontaneous recoveries without operations in a period varying from a few weeks to four months. Lesions of the pelvic girdle were observed in 29 cases. A foreign body required removal in 12 cases. Treatment should be immediate and include disinfection of the tract, removal of fragments of bone, etc., and extraction of foreign bodies. The cavity should be thoroughly explored both by radiography and radioscopy; if these are not available, every other known method of surgical exploration should be utilized. It seems necessary as soon as possible, sometimes on the first day, to make a suprapubic cystostomy. The indwelling catheter in such cases is only a makeshift. In all cases where an early operation was done, recovery followed; but, even when done later, drainage was good and cicatrization was hastened. F. Legueu (J. d'urol. méd. et chir., Paris, vii, I, 1917).

War wounds of the bladder are grave, but surgery and the retention catheter generally bring the men through. All of 29 patients recovered except 3, 2 succumbing to their extensive wounds and 1 dying later from tetanus. Immediate suprapubic cystostomy is necessary when the wound has involved the peritoneum or rectum or both, and when the anterior wall has been perforated. With a wound in the lower part of the bladder, drainage perfect, there is no need for immediate cystostomy unless fever and retention call for it.

Under other conditions the author prefers cystotomy; he deprecates further any attempt to suture the bladder wall at once unless the wound is intraperitoneal. Cathlin (Lyon chir., Jan.-Feb., 1918).

Perforation.—The fact that the intestines are, at times, perforated in twenty spots by a bullet suggests the considerable degree of care that should be given to this part of the procedure, which is carried out in the following way: The perforation nearest the rectum having been detected, the portion of intestine perforated is gently brought into full view. An assistant causes the gas in the portion of gut below the laceration to escape through the latter by slight pressure. This being done, the next step is to ascertain whether there is another perforation above. A fresh, aseptic glass tube is placed at the end of the insufflating tube and introduced into the wound with the tip directed away from the rectum. The assistant now being directed to compress the intestine below the perforation, a small amount of gas blown above the latter will inflate the upper segment if there is no opening, or indicate the location of the perforation if there is one. As soon as the latter is detected, the tube is withdrawn, the neighboring intestine on each side of the first perforation is disinfected, and the opening is closed. This procedure is renewed until all perforations have been found and closed.

This general plan renders unnecessary the removal of the intestines from the abdominal cavity during any part of the operation, the source of complications in many cases, and of death by aggravated shock in others.

Penetrating abdominal wounds made by rifle bullets are very deceiving. Many of these patients are brought in apparently in very good condition; they are able to walk and are not in pain. If nothing is done for them, often within twenty-four hours, they will have developed general peritonitis from a small leakage in the intestinal tract, and they cannot then be saved by any method. These patients should be subjected to operation at once if the wound is clearly penetrating, and many times a perforation is found where least expected from the symptoms. The distended stomach may have a perforating wound within its walls and should be carefully explored in all such cases. Patients having wounds of the liver usually recover unless there is too much destruction of tissue. Bleeding from these wounds is controlled by gauze packs. If it is difficult to control bleeding from the spleen, or if this organ is badly traumatized, splenectomy seems preferable to an attempt to repair. In wounds of the intestine, it seems much safer to repair the wound whenever possible rather than resect the intestine. Penetrating wounds of the intestine, unless operated on early, have given a very high mortality. E. S. Judd (Journal-Lancet, Nov. 1, 1918).

The manner of closing the wound is that indicated for lacerations following blows. The stomach and intestinal perforations being treated in the same way, the margins of the wound are turned inward and the serous surfaces are united by a continuous, fine-silk Lembert suture or by interrupted sutures, including the serous and muscular coats and the submucosa. These are cut short and left in, being eventually discharged *per anum.*

In simple suture of the small gut the wound must be small, with edges undamaged and mesentery intact.

Wounds by bomb fragments are ideal for suture. The wound edges were not excised, and linen thread was employed. Resection and anastomosis are indicated in the event of many perforations, extensive injuries, and mesenteric involvement. Fraser and Bates (Brit. Med. Jour., Apr. 8, 1916).

Small round perforations may be closed with a single purse-string suture of silk or linen. In larger ragged wounds, a running suture is efficient in securing accurate closure of the serosa over the defect. In extensive tangential lacerations, application of the running Lembert suture should be preceded by closure of the wound with a simple running suture traversing the entire thickness of the gut wall. In wounds at the mesenteric border, care must be taken that the perforation in the muscular coat of the intestine itself is closed. After turning in the muscularis and mucosa of the gut at the site of perforation with Lembert sutures, the opening in the mesentery is closed with a simple running suture. Complete division of the gut requires circular suture anastomosis or invagination of the ends with lateral anastomosis. The latter is the safer and amounts eventually to circular suture since the gut at the junction straightens out and assumes a nearly normal conformation. J. R. Eastman (Jour. Ind. State Med. Assoc., Nov., 1917).

Discussing thoraco-abdominal injuries involving penetration of the diaphragm, with damage to subjacent viscera, the writer states that the repair of injuries to the diaphragm should be immediately carried out or else the diaphragmatic injury is enlarged so as to deal with intra-abdominal complications. There are well-defined limits to the amount of work that can be performed upon the viscera of the upper abdomen, for with reduction of herniated viscera and repair of injuries to the liver, spleen, portions of the cardiac end of the stomach, and occasionally the colon, very little further operative

manipulation can be carried out. For injuries lower down in the abdomen it is necessary to supplement the thoracic technique with a laparotomy. Suturing of the diaphragm is comparatively simple, and after the first suture is tied it is utilized as a traction suture, and the remaining portion of the diaphragm readily sutured with a lock-stitch of No. 2 chromic catgut. C. G. Heyd (Trans. Amer. Assoc. Thoracic Surg.; Med. Rec., Apr. 16, 1921).

At times the tissues around a perforation are sufficiently contused to render an omental graft necessary.

Enterectomy is sometimes required, and not infrequently exsections of the intestine are necessary. In that case the intervening portion, if it is not too long, had better be resected, thus avoiding a double operation in the continuity of the gut.

After the active measures described have been carried out the extravasation of the contents of the stomach or intestines may make it necessary to flush the peritoneal cavity. Warm, sterilized water should be used, but care should be taken not to handle the intestines roughly. By turning the patient on his side the fluid is poured out. The abdominal cavity is then dried with large sponges wrung out of warm, sterilized water. Chilling of the viscera should be carefully avoided, and the parts should be exposed to the air as short a time as possible.

Drainage is sometimes necessary, especially for wounds of the solid viscera, such as the liver, spleen, kidneys, etc., in which active measures were not resorted to early. The weight of evidence, however, stands in favor of dispensing with drainage whenever it is possible. In bad infection large drainage tubes may be

inserted into the flanks as well as the pelvis.

> Twenty-five cases of recto-colic rupture due to compressed air were collected by the writer. The symptoms are those due to intestinal rupture and shock. Of the 16 cases operated on, life was saved in 7, including the author's 2 cases. The operative mortality is therefore 57 per cent.
>
> When the intestinal perforations are multiple, as is usually the case, and when the intestine is reduced to its mucosal coat alone, suture is useless.
>
> If the condition of the patient is poor, the intestine should be brought to the surface and fixed to the abdominal wall to form an **artificial anus.** If this is not possible, an **enterectomy** with a **colo-colic** or **colo-rectal anastomosis** is indicated. In the writer's cases such anastomosis was impossible because of the condition of the rectum. The upper stump of the colon was therefore fixed to the abdominal wall as a permanent artificial anus. Both patients made good recoveries. G. Jean (Presse méd., xxix, 675, 1921).

To summarize: we will say that immediate exploration of the abdominal cavity is indicated as soon as it is suspected to have been penetrated or in any way injured by a traumatism. The injury to its contents must then be repaired under strict aseptic precautions.

Should no lesion be found, the mere exploration should result in no serious damage.

After-treatment.—Food should be withheld for thirty-six hours, but a little **water and brandy,** in teaspoonful doses, may be allowed, especially if there is any degree of shock. In that case it is advisable also to use **stimulants** by the rectum or subcutaneously. **Nutritive enemata** of beef-tea and milk are necessary to sustain the patient's powers.

Proctoclysis of normal salt solution according to the Murphy gradual method should be resorted to. The head of the bed should be raised to apply the Fowler principle favoring the gathering of secretions in the pelvis, where the absorption is less rapid.

During this procedure no food should be given by the mouth. If the patient is weak, rectal alimentation is indicated. In the less severe cases liquid food may be permitted by the evening of the second day, and soft, easily digested food after a week, rectal alimentation being continued until then.

The sutures can be removed on the ninth day. The closure of the external wound must be complete before the patient can be allowed to leave his bed, and the danger of a ventral hernia should be counteracted by means of an abdominal supporter.

Hypodermic injections of **strychnine,** $\frac{1}{60}$ to $\frac{1}{30}$ grain, three times a day, according to indications, will prove most effectual in maintaining the strength of the patient and toning the muscular wall of the intestine.

<div align="right">Ernest Laplace,
Philadelphia.</div>

ABORTION.—DEFINITION.

—*Abortion* is the expulsion or removal of the fructified ovum before the fetus is viable,—meaning by the term "viable" that the fetus has reached such a stage of development that it can live, thrive and grow after birth. We cannot say definitely when the fetus reaches that stage, but it has been the custom to consider that it

becomes viable at the end of the seventh lunar month or the twenty-eighth week of pregnancy.

Still, a very young fetus may breathe after delivery. This occurred, for example in 3 cases (2 in the fifteenth and 1 in the nineteenth weeks, respectively) reported by Glöckner. In the first of these there were six respiratory movements before and five after severing the cord, the fetus living one hour. In the second case the fetus lived an hour and a half and breathed five times. The third fetus lived but half an hour and breathed eight times. The autopsy showed air in the stomach, but the lungs were empty.

From a clinical standpoint, however, the fetus is not viable before the end of the seventh calendar month.

Premature labor or delivery means the termination of pregnancy between the end of the seventh month and full term. In certain cases it is difficult to distinguish between late abortion and early premature labor.

As to the time of occurrence, it has seemed convenient to consider two varieties: *early abortion,* when it occurs before or about the end of the third month of pregnancy, and *late abortion,* when it occurs between the latter part of the third month and the end of the seventh month of pregnancy.

Three varieties as to the methods of occurrence are also recognized: the *spontaneous,* when the abortion occurs without any outside interference, and is caused by some abnormal condition of the mother or fetus; the *accidental,* when the abortion is due to accident; and the *induced,* when the abortion is produced artificially by interference from outside. Induced abortion is deemed legitimate when it is produced by a physician for just cause. The cause is considered just only when the abortion is induced to save the mother's life which otherwise is imperiled. When the abortion is induced without such just cause, that is, when it is done for improper or immoral reasons, whether by the mother or the professional abortionist, it is known both from a medical and legal standpoint as *criminal abortion.*

In the author's clinic during the past 6 years, in a total of 5500 cases, he has had to perform abortion only 31 times. Again, although 134 women came to the clinic for therapeutic abortion as follows: (1) of their own accord, 55; (2) sent by physicians, 72; (3) sent from the intern clinic, 4; (4) sent from the obstetric dept. 3, only 30 had to be operated upon.

The author holds that at least two-thirds of the therapeutic abortions performed by private physicians are not indicated and are unnecessary when the cases are dealt with by skilled obstetricians. This is the evil practice that must be suppressed. On no account should therapeutic abortion be included among legitimate obstetrical operations.

There is scarcely any agreement among competent physicians as to the causes which are strictly indicative of induced abortion. In every case where an abortion is considered a consultation should be held with a special internist who would not be concerned with the pregnancy but with the absolute condition of the woman as to concomitant disease. The author recognizes that 80 per cent. of abortions have their initiative from the woman herself. G. Winter (Zeit. f. Gynäk., Jan. 6, 1917).

Criminal abortion, according to the writer, a professor in the university law department, should be classed with espionage, counterfeiting, anarchy, etc., as the crime against society is more important than the

individual character of the crime. The birth-control propaganda should be suppressed, as the arguments in favor of birth control apply also to voluntary abortion. Criminal abortion cases should not be given a jury trial, as the jurymen do not realize the social danger of the crime, and they yield to intimidation by the abortionists, usually powerful and always with a protecting backing. Another point which he emphasizes is that a physician cited in a suit for criminal abortion should be relieved of the ban of professional secrecy, so that his testimony can be used against the abortionists. Berthélemy (Bull. de l'Acad. de Méd., Paris, Sept. 4, 1917).

The writer deprecates the modern tendency to enlarge the indications for induced abortion. The medical indications have still more been reinforced by social and economic consideration, without speaking of the pressure brought to bear on the medical man by the patient's relatives when pregnancies are too frequent. Of 202 cases sent to his clinic for therapeutic abortion, only 59 were performed there in the lapse of 5 years. The reason for this condition of affairs is due to a change in ethical ideas in Germany. Bumm (Berl. klin. Woch., Jan. 7, 1918).

As to frequency, it is impossible to estimate even approximately the proportion of pregnancies terminating in spontaneous abortions. Women who object to having large families have such a multitude of expedients to cut short their pregnancies, and frequently conceal their methods so carefully, that our estimates as to percentages cannot be exact. From the results of our experience in private practice it is indicated that abortion occurs from accident or spontaneously in 1 out of 10 pregnancies, that is, 10 per cent. However, if we include induced abortions (legitimate and criminal), it is probable that abortion occurs in 3 out of 10 pregnancies, that is, in 30 per cent.

The figures of the Paris Maternité from 1897 to 1905, as collected by G. Rimette, show 9875 pregnancies, 1457 abortions, 627 spontaneous abortions, 414 complicated abortions, 367 infected abortions, and 27 deaths from abortion.

Michailoff, who bases his figures on 257,988 births in one of the Russian maternities, found that the proportion of abortions to full-term deliveries was about 1 to 10. Keyssner, in his polyclinic material, found 469 abortions to 2623 confinements, or 1 to 5.6.

Miscarriage.—We consider abortion and miscarriage are synonymous terms. In former times the terms were not considered so, nor are they now in some quarters. Many, if not all, of the Rotunda men, and some obstetricians of North America, still use the term miscarriage in the old-fashioned way. According to them, miscarriage is a term applied to the expulsion of the ovum between the beginning of the fourth and the end of the seventh month, that is, between the time of the complete formation of the placenta and the time that the fetus becomes viable. Those who thus define miscarriage say that abortion is the term applied to the expulsion of the ovum before the end of the third month, that is, before the formation of the placenta has been fully completed.

SYMPTOMS.—The symptoms of abortion are hemorrhage, a brown discharge after the death of the ovum, pains in the pelvis, complete or partial dilatation of the os uteri, expulsion of the whole or part of the ovum.

The hemorrhage in the majority of abortions is not profuse, and may continue a long time. In a certain class of cases, however, the hemorrhage is very profuse and sometimes causes death.

Some obstetricians think that hemorrhage in early abortion is never profuse enough to cause death. Certainly the hemorrhage before the formation of the placenta is seldom dangerous to life. There are exceptions to this rule, however; but, so far as we know, the majority of the fatalities from hemorrhage in early abortion occur in cases of criminal abortion where sharp or pointed instruments are used.

In considering the symptomatology of abortion, however, it is very important to obtain a clear conception of the two varieties commonly recognized, viz.: the "threatened" and the "inevitable."

[The importance of this distinction asserts itself in connection with treatment. In the case of threatened abortion we are in doubt as to whether the uterus will be emptied or not, and our treatment aims at controlling the influences which are producing the symptoms of abortion, such as hemorrhage and uterine contractions. In the case of inevitable abortion the contents of the uterus will be held or partially expelled by nature's efforts, and we pursue a line of treatment entirely different from that adopted for threatened abortion. Our aim now is to assist nature in expelling the contents of the uterus as soon as possible with safety to the mother. A. H. WRIGHT.]

The symptoms of *threatened abortion* are hemorrhage, pelvic pain and perhaps a slight dilatation of the os, especially in multiparæ. The hemorrhage, as already mentioned, is comparatively slight in a large proportion of cases, and may continue for nine or ten weeks or longer without ending

in actual abortion. The pains which are caused by uterine contractions may be fairly severe and may continue for some time without causing the expulsion of the ovum.

In inevitable abortion there are also hemorrhage, pelvic pains and more or less dilatation of the os, but these phenomena are more severe and pronounced. It is sometimes, in fact, very difficult to decide when an abortion becomes inevitable. Probably the safest guide is the hemorrhage. If the fetus is dead, or if the membranes are ruptured, abortion is also deemed inevitable. No definite line of demarcation can be established in this regard.

The symptomatology of abortion varies, of course, to a certain extent according to the time at which it occurs. As carefully collated by Lutaud, of Paris, the symptoms at the different periods are briefly as follows:—

Abortion During the First Month. —This usually gives rise to symptoms simulating those of retarded menstruation. Slight pains in the back in the region of the uterus are complained of; the symptoms, in this particular, resemble those of normal labor, but are very much less marked. Blood, blood-clots, and flakes of the mucous membrane of the uterus are gradually expelled during several days. The ovum is expelled entire, but it is so small that it is discovered, as a rule, with great difficulty.

Abortion During the Second Month. —Inasmuch as the uterus has decidedly increased in size as compared with its size in the first month, the contractions and pains are comparatively stronger. The embryo is usually expelled inclosed in the unbroken

membranes. Sometimes, however, the latter are ruptured.

The embryo and membranes may be detached from the uterus in two ways:—

(*a*) By hemorrhage between the membranes and the uterus, followed by uterine contraction.

(*b*) By contraction of the uterus, followed by hemorrhage. In the latter case the abortion is more prolonged, the membranes being detached but slowly from the uterus.

If the embryo be still living, the abortion lasts longer, and the hemorrhage is greater. If the embryo be dead, the whole is usually expelled like a foreign body, and without rupture of the membranes.

Examination of the uterus will show that it is increased in volume and situated lower down in the pelvis than normally. The cervix is dilated, softened, and filled with blood-clots. The dilatation is more marked in multiparæ than in primiparæ.

The cervix, though dilated, does not become effaced, and the embryo contained in the unruptured membranes may pass through the cervix and be expelled. If the membranes are ruptured, however, the embryo passes by itself, the very thin umbilical cord breaks, and the cervix closes. The membranes are, in this latter case, expelled later on. The membranes are ruptured about once in every 2 cases.

Abortion from the Beginning of the Third to the End of the Fourth Month.—This occurs nearly always in two stages, the first consisting in the expulsion of the fetus, and the second in the expulsion of the membranes and placenta.

The cervix in this form of abortion tends to diminish in length. The uterine contractions act more powerfully than in the previous forms of abortion. Under their influence the membranes are ruptured and the fetus is expelled.

The placenta may still be adherent; the cervix then closes again, and the placenta and membranes are expelled later on. Hemorrhage is likely to accompany the delivery of the placenta and membranes, especially when the former is only partly detached. Under these circumstances each uterine contraction is accompanied by hemorrhage.

The placenta may be already detached when the fetus is expelled; in such a case it is likely to be expelled immediately after the latter, before the cervix closes, but part of the decidua may remain in the uterus after delivery of the placenta. This occurs most frequently when the fetus is dead.

Statistics show that retention of the placenta occurs most frequently during this period.

Abortion During the Fifth and Sixth Months.—The fetus and placenta are almost always expelled separately. Uterine contraction is more marked; the cervix tends to become more effaced and to dilate.

Delivery of the placenta usually follows delivery of the fetus rapidly, and the tendency to hemorrhage is less marked than in the previous forms of abortion.

Of 501 cases of abortion analyzed by Varnier and Brion, the fetus, or embryo, and the placenta were expelled separately in 453, and together in 48 cases. When the delivery occurred in two stages, the time found to elapse between the expulsion of the

fetus and that of the placenta was as follows: 120 cases, within 15 minutes; 81 cases, from 15 to 30 minutes; 78 cases, from 30 to 60 minutes; 83 cases, from 1 to 4 hours.

Whenever the placenta and membranes are not expelled within four hours after the expulsion of the fetus, or embryo, there is retention of the membranes and placenta.

Abortion may take place suddenly, or resemble, in that particular, the irregular periodicity of normal labor, with more or less hemorrhage. It may, indeed, last several days, owing to weakness of the uterine contractions or adhesions to the uterus or retention in the cervix of the masses to be expelled. (Rokitansky, Schülein.)

Sudden or rapid abortion is frequent during the first two months; when the expulsion takes place after the third month it generally presents the characters of normal delivery.

The menstruation returns earlier after abortion than after a normal labor. Engländer, in a recent (1906) study of 57 cases of abortion, undertaken to ascertain the period of their first subsequent menstruation, found that in 64.9 per cent. the menses reappeared in four weeks; in five weeks in 14 per cent. The remainder varied, 1 patient going as long as six weeks after the abortion before menstruating. After labor, it is usually six to eight weeks before patients menstruate.

DANGERS.—Just as parturition may be attended by deviations from the normal, so may abortion.

Retention of the placenta occurs frequently. The latter is sometimes expelled safely after some days, either entire or in pieces, but prolonged retention exposes the patient to hemorrhage, toxemia, and septicemia. When completely detached, though retained, the placenta gives rise to no hemorrhage, but if only partially detached such is not the case and copious hemorrhage may thus be produced.

In 15,000 cases of abortion studied by Seegert, fever occurred in 15 per cent. Of 633 patients, 182 had chills before they came under active treatment. Among the 15,000 patients were 450 who were severely infected; of these 94 died. In 82 cases autopsy was made. Those cases showed the most severe symptoms in which the longest time elapsed before the uterus was completely emptied. Fever often ceased when the uterine contents were expelled.

The general symptoms that follow hemorrhage (a weak pulse, vertigo, fainting, etc.) occur only when the loss of blood has been severe. Under these conditions septicemia, as evidenced by fetid lochia, chills, and high temperature, is a probable complication. Endometritis, salpingitis, and peritonitis have also been witnessed under such conditions. Tetanus is also another possible complication of these cases. Sterility commonly follows induced abortion.

The writer observed 8 cases of sterilization, the result of induced abortions. All the women were married, in good health and none over 35 years of age. In each instance the abortion was induced soon after the first period had been missed, usually the second or third week. The abortions induced in these women were as follows: 3 had been relieved 5 times in 2 years; 2 six times in 2½ years; 1 woman 9 times in 3 years; 1 woman 11 times in 5 years; 1 woman 14 times in 5 years. In later years when these women desired to

have children they found themselves sterile. They cheerfully submitted to treatments which buoyed them with hopes from month to month, only to find that at the end of their course of treatment they were just as sterile as they were before they consulted the gynecologist. Reder (Trans. Amer. Assoc. of Obstet. and Gynec.; N. Y. Med. Jour., Nov. 23, 1918).

ETIOLOGY AND PATHOGENESIS.

—There has been much theorizing as to the causes of abortion, and in many instances, the explanations and complicated classifications vouchsafed have obscured the subject instead of elucidating it.

In a study of 164 instances of abortion, out of 563 patients examined, the writer found that more than 20 per cent. probably over 25 per cent., were induced. Sixty per cent. of all induced abortions result in more or less permanent sterility. These are worst when caused by the midwife, the patient herself, and last by the physician. A positive Wassermann is obtainable in about 25 per cent. of all women who have aborted. Less than one-third of these give any history or show any physical signs of the disease. Syphilis interrupts pregnancy at any and all periods of gestation, and in more than 60 per cent. of pregnancies. Renal deficiency does it only in the event of renal decompensation at any period of gestation. G. D. Royston (Amer. Jour. of Obstet., Oct., 1917).

It is generally recognized that the causes may be of maternal, paternal, and fetal origin..

The causes of abortion may be classified as follows: 1. Criminal provocation, direct or indirect. 2. Maternal, such as constitutional disease, pelvic disorders, affections of the nervous system, etc. 3. Paternal, such as certain constitutional diseases, chief of which is syphilis, and old age. 4. Fetal, such as death of the fetus and diseases of the placenta.

It is generally supposed that 50 per cent. of abortions are criminally provoked. Titus found 82 per cent. of a series of criminal abortions at the Johns Hopkins Clinic were incomplete, and 78 per cent. of this same series were infected, streptococcus infections occurring in 34.3 per cent. of these cases.

Under the maternal, paternal and fetal causes of abortion, syphilis is the most frequent cause. In 657 syphilitic women there were 35 per cent. of abortions.

Decidual endometritis is a cause of abortion in 52 per cent. of infected and 68 per cent. of uninfected cases, while retroposition is a cause in 30 per cent. of the cases. Lacerations of the cervix and pelvic floor account for 14 per cent. of all abortions. Cancer and intra-uterine tumors are frequent causes. Poisons in the maternal blood from fevers such as smallpox, scarlet fever, typhoid and the like, are frequent causes of abortion, as are affections of the nervous system, as chorea, epilepsy and shock. Epidemic abortions caused by the bacillus abortus of Bang and streptococci have been reported.

The causes referable to the fetus include all the many diseases of the placenta, death of the fetus, and syphilis. The paternal causes include mainly syphilis, gonorrhea, albuminuria, lead poisoning, and old age. J. E. Davis (Jour. Mich. State Med. Soc., xvii, 2, 1918).

Maternal Causes.—Most cases of abortion are generally attributed to traumatisms, falls, blows—a cause not infrequently met with in the slums— the likelihood of premature delivery being decreased in proportion as the blow or other injury is remote from the region of the uterus. Operations, even sometimes when insignificant, have produced abortion. The so-called "aborting habit" is also recognized as a potent factor in this connection ; but this expression doubtless

covers, in most instances, some hidden and probably removable cause.

The predominating cause, however, according to statistics, is syphilis, to which are attributed over one-fourth of the cases. When it is contracted before conception, abortion occurs repeatedly—early when the infection is of recent date, but gradually nearer term as the contamination is more remote. There comes a time, therefore, when normal delivery becomes possible.

The prevailing view that syphilis is a prominent factor in the causation of abortion has been denied by Trenchese and others. In a summary of 679 cases of abortion at the Michael Reese Hospital the writer also found that syphilis was an etiological factor in but 4 per cent. of abortions. Lackner (Surg., Gynec. and Obstet., xx, 537, 1915).

In a study of the causes of abortion 563 patients were examined. A history of abortion was elicited in 178. The 164 selected for detailed study gave a grand total of 664 pregnancies, 348 of which ended in abortion. Criminal abortion was the most common factor in the series; 51 out of 164 women having confessed to an induced labor, many repeatedly. These 51 women had in all 220 pregnancies of which more than half, namely 118 (52.4 per cent.) resulted in abortion. Of these 118, 84 (71.1 per cent.) were frankly acknowledged to have been induced. Comparing the percentage of induced abortions with the abortions in his entire material, the writer arrived at the figure 23.8 per cent. Only 20 (39.2 per cent.) produced living children after having had abortions induced. Only 10 out of the 51 patients had normal genital organs; the remaining 41 were more or less permanently disabled. Among the 164 cases, 46 gave a positive Wassermann and 5 patients with definite histories gave negative reactions after having

been treated. The writer holds that abortions are caused by syphilis much more frequently than the medical public realizes. Royston (Amer. Jour. of Obstet., Oct., 1917).

Next in order are malpositions and inflammatory disorders and tumors of the uterus and its adnexa, including ovarian cysts. Laceration of the cervix has recently attracted attention as a cause of abortion. The tear may be limited to the cervix, or it may extend upward to the body of the organ; or again the rupture may occur above the external os.

Charpentier refers to three distinct local uterine conditions in otherwise healthy women: 1. Ill-developed uterus; the muscular coat does not readily soften, yet remains very irritable. Rare. 2. Displacements, especially flexions. Spur at the angle of flexion hypertrophies interferes with uterine development. 3. Congestion of the body and cervix, due to idiosyncrasies. Endometritis.

Debilitating influences of various kinds, such as insufficient food, excessive physical labor or fatigue, mental and physical shock, the abuse of alcohol, tobacco (women employed in cigar, cigarette, etc., factories), carbonic oxide (as shown by the frequent occurrence of abortion in cooks) and lead, including paternal intoxication by this metal, tend also to bring on miscarriage.

Great shock or injury is sometimes better borne by pregnant women than frequently repeated shock, e.g., the use of the sewing machine with the foot. Davis has reported cases illustrating the fact that motoring during the early months of pregnancy is frequently followed by abortion. The danger seems to lie in the fact that the rapid motion of a motor car subjects the patient to many small, frequent jars. The characteristic of abortion

following motoring is its slow and insidious development without bright hemorrhage or pain. These abortions are, as a rule, incomplete, and require curetting. While motoring is dangerous in early pregnancy, in the later months of gestation and with reasonable precautions as to smoothness of roads and moderation of speed it may prove exceedingly useful. EDITORS.

Debilitating diseases have also been found to induce it. Influenza, in which the general adynamia is marked, has been recorded as a cause. In Asiatic cholera, abortion is almost invariably produced.

> The view that *Bacillus abortus* (Bang) is pathogenic for human beings is not proven, although it is possible to cause antibodies for *Bacillus abortus* to appear in the blood-serum of adults by feeding a milk which is naturally infected with *Bacillus abortus* and which contains the *Bacillus abortus* antibodies. Cooledge (Jour. Med. Research, July, 1916).

> The writer found that complement fixation reactions with the polyvalent antigens of bacillus abortus (Bang) and bacillus abortivo-equinus and the sera of 50 women aborting in the early months of pregnancy yielded negative results. Williams and Kolmer (Am. Jour. of Obstet., vol. lxxv, p. 194, 1917).

A bacillus has been incriminated by Bang as a cause of abortion, but it is not receiving much support.

Conversely, conditions which tend to exaggerate the contractility of the uterine muscle are also recognized causes. Ergot, copper sulphate and other "abortifacients" are familiar agents of this class. This evil action has also been attributed to quinine, but there is reason to believe that this valuable remedy should not be withheld in pregnant women, when indicated therapeutically, especially in view of the fact that malaria itself tends to cause abortion. Thus, in a study of the action of quinine on pregnant women, Frederici found that in 49 pregnancies quinine had been used in 47, the patients suffering more or less severely from malarial fever; 47 terminated at the usual period by the birth of a chlid, and 2 aborted. In these 2 cases he deems it extremely probable that the high fever from which they suffered was instrumental in producing abortion. He concluded that medicinal doses of quinine were powerless to induce abortion.

> The writer collected 14 cases of severe poisoning from nitrobenzole used as abortifacient. The earliest, which occurred in 1866, was in a girl of 18 who, when 5 months pregnant, took 10 grains of the drug. Pregnancy was not interrupted but the girl was severely poisoned with cyanosis as a prominent symptom. The cases showed that nitrobenzole is without any abortifacient properties and can destroy fetal life only when the mother is fatally poisoned. Spinner (Corresp. Blatt. f. schweizer Aerzte, Oct. 27, 1917).

Infectious diseases provoke abortion in a large proportion of cases when the febrile period is reached. It occurs in about two-thirds of pregnant women attacked by typhoid fever, especially during the earlier months. Uterine hemorrhage is usually the first symptom observed. Thus Sacquin collected 310 cases, and found abortion in 199; while Martinet found 66 abortions in 109 cases.

Small-pox causes abortion in about 40 per cent. of the pregnant women it attacks and the mortality is about 50 per cent., but is nearly 100 per cent. in the confluent type. In varioloid the child sometimes remains unaffected. The disease may also develop during convalescence. Abortion dur-

ing variola is apt to be attended with more than the ordinary hemorrhage.

Arnaud has reported several serious cases occurring during convalescence after small-pox. The grave symptoms are attributed to the retention of the fetus, which died during the acute stage of small-pox, and was frequently only expelled during or after convalescence.

Measles is an infrequent complication of pregnancy, but, as observed by Klotz, it causes abortion in the majority of such instances. Pneumonia frequently appears as an additional complication. Scarlatina is also infrequently observed in pregnant women, though it occurs commonly as a complication of the parturient state.

Pneumonia causes abortion in about one-third of the pregnant women it attacks early and in two-thirds of those which contract the disease late. In the latter cases the fetus, though viable when born, may soon die of the infection after birth. The statistics of 213 cases of pneumonia during pregnancy published by Flatté showed that the pregnancy was interrupted in 118 cases, there being 42 abortions and 76 premature deliveries. Death of the mother occurred in 75 cases among the 213: a mortality of 35 per cent. The mortality of the mother was greater in premature deliveries than in abortion.

Pulmonary tuberculosis, owing to its exhausting influence upon the nutritional resources of the body, renders it unfit to carry the fetus to term when the morbid process is far advanced. Abortion is relatively frequent in such cases, its occurrence and the viability of the child depending upon the stage of the disease.

In 385 cases in which others advised interruption of pregnancy the writer was able to escape it in 278 instances.

Only when cough, nightsweats, evening fever, and loss of weight continue in spite of sanatorium treatment is abortion indicated.

After the first 3 months, he intervenes only if the lung process is mild or only recently flaring up; otherwise one cannot hope to influence the disease.

If patient has several living children, or if there is laryngeal tuberculosis, or this is the first pregnancy in far advanced tuberculosis, he interrupts pregnancy and sterilizes the woman. With acute heart disease during a pregnancy he advises that the uterus be emptied by **anterior colpohysterotomy** under **lumbar anesthesia** after the acute manifestations have subsided. Von Jaschke (Monats. f. Geb. u. Gynäk., Apr., 1920).

Chorea, though a rare complication of pregnancy, causes abortion in one-half of the cases, and is especially observed in primiparæ. If the delivery occurs sufficiently late, the child may live, but is frequently affected with chorea. The chorea sometimes ceases after delivery.

Cardiac diseases influence pregnancy when it is sufficiently marked to impair the general circulation. Acute pericarditis practically has no morbid influence on gestation, but chronic pericarditis is deemed pernicious. Acute endocarditis assumes increased virulence during pregnancy, its tendency being to become ulcerative, and to entail a fatal ending.

Icterus, in its various forms, sometimes complicates pregnancy. Even simple catarrhal icterus may cause abortion, but in icterus gravis it occurs always and usually proves fatal. In the epidemic icterus of pregnancy, the probability that abortion

will occur is somewhat smaller, while the mortality is not as great. Pregnancy not only aggravates even simple icterus, but it increases the tendency to yellow atrophy of the liver.

Paternal and Fetal Causes.—The influence of syphilis on abortion has been reviewed; in most instances it is acquired from the male directly, either before or after conception, the disease being communicated to the fetus, in the latter case, through the placenta. In accord with Colles's law, the fetus may, as is well known, inherit the paternal syphilis, while the mother remains immune. Abortion may thus be caused through maternal or fetal syphilis acquired from the father.

Any condition such as senility, alcoholism, overwork, etc., which tends to lower the vitality of the father tends also to weaken the offspring and promote the tendency to miscarriage in the mother. Certain occupations which expose the patient to the action of certain poisons, mercury, phosphorus, or lead, for instance, tend in the same direction.

Besides the features which tend to compromise the development of the fetus that have been referred to, it is itself subject to injuries communicated from the exterior, blows, shocks, penetrating wounds (knife, bullets, etc.), etc. The application of X-rays has recently been added to the list of known causes.

Low or vicious attachment of the placenta, degeneration of the chronic villosities, hydramnios are the remaining main abnormalities which affect directly the fetus and cause its premature elimination by the uterus.

PROGNOSIS.—Considerable loss of blood may occur in a case of threatened abortion, and yet the patient, when properly treated, proceeds to full term. Cases of spontaneous abortion unattended by complications practically always recover. The degree of antisepsis has much to do with the result however; while, for example, in Pinard's service where rigorous asepsis was observed the mortality was only 0.81 per cent.; corresponding cases (which included favorable and unfavorable) outside his services reached 27.5 per cent. Out of 610 cases treated at the Boston City Hospital in 10 years; 29 deaths, or 4.75 per cent. They included a large proportion of induced and neglected cases. The deaths include cases with pre-existing typhoid and pneumonia. With two exceptions those of the 29 deaths obviously due to the miscarriage were caused by septic pneumonia following a miscarriage between 4 and 6 months.

TREATMENT.—**Treatment of Threatened Abortion.**—When the symptoms of threatened abortion appear we should endeavor to stop the morbid process, especially when the hemorrhage is not copious, the pains are not severe, and there is no evidence of the escape of liquor amnii. Our chief aim should be to keep the patient absolutely quiet, by ordering her to bed, and relieve the pains due to uterine contractions by means of opiates in suitable doses. **Opium** seems to be better than morphine, even when the latter is given hypodermically. The tincture of opium, 30 minims (2 Gm.) should be given by the mouth, followed by 15 minims (1 Gm.) every hour, repeated three or four times if required. Or, better still, 2 grs. (0.13 Gm.) of the aqueous extract of opium can be given as a rectal suppository, and 1 gr. (0.065

Gm.) every hour afterward, three or four times if needed. If **morphine** be preferred, ½ gr. (0.032 Gm.) may be given hypodermically, and ¼ gr. (0.016 Gm.) every hour, therefore, for three or four doses if required. An excellent plan when one wishes speedy effect from the opiate is to give at once ½ gr. (0.032 Gm.) morphine hypodermically, and 15 minims (0.92 Gm.) of tincture of opium by the mouth every hour afterward, or 1 gr. (0.065 Gm.) of **extract of opium** in a suppository every hour afterward for three or four doses if required.

[Some physicians will consider that such dosage is large. Many physicians and obstetricians grew timid about the use of opium because of the violent antiopium riots that broke out in many surgical camps about twenty years ago, after Lawson Tait told the abdominal surgeons of the world that opium was an abomination which must be discarded in their work forevermore. The pendulum has turned, however, and is going the other way. A. H. WRIGHT.]

We ought, of course, to consider that opium should be given with great care. At the same time, the writer thinks it absurd to give, for instance, 10 minims (0.61 Gm.) of tincture of opium by the mouth, three times a day, for the pains of threatened abortion. As a rule such doses will have no good effect, because they will not relieve the pains, and they may have a bad effect by causing constipation. Opium does cause constipation, and thus interferes with elimination, but the writer does not admit that it causes complete paresis of the intestines. Sepsis alone causes that kind of paresis.

The constipation caused by opium can be easily overcome by the administration of ordinary **laxatives.** If,

however, the physician who has given opium in the case of threatened abortion is afraid to use mild cathartics for constipation, he might order an ordinary **enema.**

Some years ago the administration of **viburnum prunifolium** was supposed to have a good effect in cases of threatened abortion. The result of recent experience does not indicate that such supposition is correct. The writer considers it practically worthless. The fluidextract, ½ to 1 dram every three hours, or 10 drops every hour, with **chloral hydrate** 8 grains, have, however, been found effective in arresting uterine contractions when opium could not be used or when its constipating effects might prove detrimental. Or, **chloral hydrate,** 10 grains, and **potassium bromide,** 20 grains every two or three hours, may be preferable, since the hypnotic tends to insure the absolute rest and quiet that should be observed to obtain a satisfactory result. **Codeine** is preferred to other opiates by some obstetricians.

Treatment of Inevitable Abortion. —There never has been, and probably never will be, a consensus of opinion among obstetricians as to the treatment of abortion. It seems convenient to consider that there are three general plans: expectant treatment, treatment by tamponade, forced dilatation of the cervix and curettement.

Expectant Plan.—The term expectant is not a good one as a rule, and it becomes most unsuitable if it is misunderstood.

Lusk was perhaps the most prominent advocate of the expectant plan of treatment. He urged that, when in the third month the ovum is thrown off without the rupture of the membranes, the hemorrhage rarely as-

sumes dangerous proportions, and explained how the uterine contractions sometimes pressed the ovum into the cervix. During these uterine contractions the ovum descends and the upper portion of the body of the uterus retracts. Some coagulation of the blood takes place between the ovum and the retracted uterine walls, while the ovum forms a tampon which fills the cervix like a ball valve, and thus restrains the hemorrhage. When there is no interference, the

Ovum, five weeks.

ovum, after being retained for a time as described, is frequently expelled entire, leaving the uterus in the best possible condition for satisfactory involution. In such cases, and they are by no means uncommon, nature has done well. Why should we try to improve or interfere with such magnificent work?

Opinions still differ greatly as to whether active or conservative measures are preferable, but at the Strassburg clinic, in charge of Fehling, active treatment is the usual course. A very important guide for the management of the case is what she calls "latent complications," namely, that while nothing pathologic can be palpated, yet the patients complain of pains during internal examination. Tenderness of the vaginal portion of the uterus or tissues around indicates incipient inflammation, showing that the morbid process is not restricted to the endometrium but is extending beyond it. This calls for strict conservative treatment, just as much as exudation in the pouch of Douglas or disease of tube or ovary. B. Engler (Corresp. Blatt f. schweizer Aerzte, July 21, 1917).

Removal of the Uterine Contents. —It should be definitely understood that, while nature is doing good work, we should watch carefully, and be ready to assist when her efforts have ceased to be efficacious. When the os and cervical canal are sufficiently dilated to allow the introduction of the finger into the uterine cavity, and the uterine contents are not extruded, we should interfere, and endeavor to empty the uterus. We should presume, unless there is positive proof to the contrary, that the ovum is intact, and should not be broken.

The following course is recommended: Place the patient across the bed, in the lithotomy position, and with the external hand endeavor to depress the uterus through the abdominal wall until the index finger of the other hand (carefully asepticized) can be passed through the os and up to the fundus. An anesthetic is only occasionally required. Pass the finger up on the lateral wall of the uterus until it is above the ovum, at or near the opening of one of the Fallopian tubes; then pass it across the fundus to the neighborhood of the other Fallopian tube, and sweep down this wall, driving the contents of the uterus before it. In these manipulations try to avoid rupturing the

ovum. If unable to remove the uterine contents in the way described, one should try the following Rotunda procedure: Take the finger out of the uterus and place it under the fundus, that is to say, in the anterior fornix if the uterus is normal in position, and in the posterior fornix if the uterus is retroverted. Sink the other hand into the abdomen and compress the body between the two hands. The ovum is then driven out of the uterus into the vagina and removed (Jellett).

It is well to remember that there is a period between early and late abortion—say, in the latter part of the third month—when it is difficult, with the finger-tip, to make out the placenta, because it feels exactly like the endometrium. It is possible under such circumstances to make the mistake of imagining that the uterus is empty while the thin, broad placenta is completely adherent. In such a case it is better to try to remove this placenta by scraping with the finger-tip, as the use of the metallic curette under such circumstances is dangerous.

> Analysis of 750 cases of abortion of the out-patient department of the Chicago Lying-in Hospital, and treated at their homes. The routine treatment adopted in the 276 cases of threatened hemorrhage was absolute **rest** in bed, with **morphine** and **codeine** every four hours, with **saline purgatives** where needed. When malposition of the uterus was present, this defect was corrected. The pregnancy was saved in 72.8 per cent. of the cases. The inevitable abortions were treated by **packing** and **curetting** with the finger when possible, using the curette only when absolutely necessary, excepting in chronic cases. All the mothers recovered.
>
> Summary of conclusions: Absolute

> rest was imperative; blood loss should always be prevented: cotton pledgets are preferable for tampons to gauze, being firmer; whenever possible emptying of the uterus should be done with the finger; laminaria tents are difficult to sterilize. Stowe (Surg., Gynec. and Obstet., Jan., 1910).
>
> Divergent views continue to exist regarding the relative advantages of active and conservative treatment in non-septic abortion. According to the writer, **curettage** is necessary in 40 per cent. of non-septic cases treated expectantly.
>
> The curettage insures an empty uterus, prevents subsequent bleeding, shortens the patient's stay in the hospital, and is relatively harmless. D. S. Hillis (Surg., Gynec. and Obstet., xxxi, 605, 1920).

The Tampon.—The vaginal tampon (or plug, as it is still termed by many in Great Britain) has been used for various obstetrical purposes for centuries. We believe that treatment by tamponade is the safest and best kind in all varieties of inevitable abortion, whether complete or incomplete.

There are two kinds of tamponade: the vaginal and uterovaginal.

Vaginal Tamponade.—In order to be efficient the vaginal tamponade should be properly done. Although it is one of the simplest of obstetrical operations it appears that in the majority of cases it is imperfectly carried out. In the first place the vagina cannot be properly plugged while the patient is lying on her back, or on her side. The patient must be put in the Sims (semiprone) position. The perineum and pelvic floor must be thoroughly retracted by a Sims speculum, and the vagina properly ballooned, so that its vault, thus distended, may be completely filled by the material used for the packing. It is only necessary to pack tightly the upper two-thirds or

three-fourths of the vagina. The mistake commonly made of packing tightly the entrance of the vagina generally causes great pain, and frequently retention of urine, by pressure on the urethra.

The tampon checks the hemorrhage, dilates the cervix, assists further separation of the ovum by damming back the blood, and induces uterine contractions. The writer, like Smellie, prefers an antiseptic plug, and uses
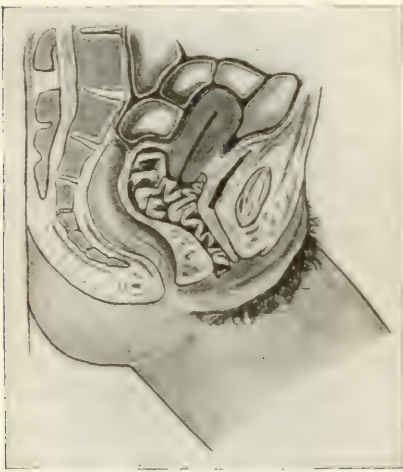
Vagina balléma (gauze packing).

material impregnated with 5 per cent. iodoform. A simple sterile plug is introduced by some, but an antiseptic plug is better. The former becomes foul in about twelve hours, while the latter (when iodoform is used) remains sweet for two or three days. The ordinary iodoform gauze is not suitable however, because it is too coarse in texture, that is, too much like a sieve. The blood easily runs through it. Therefore, the writer prefers to use a rather fine cheesecloth impregnated with the iodoform.

[It is prepared for me by Miss Margaret Lash, as follows: Take 4 yards of cheesecloth (good quality) 27 inches wide; tear (not cut) into strips 4½ inches wide and full length; sterilize these strips, and then boil in sterile water; wring them as dry as possible (having hands covered by sterile gloves) and thoroughly saturate them in the following preparation: 8 ounces of a 1 per cent. solution of carbolic acid in sterilized water, and enough Castile soap to make suds; 3 drams and 1 scruple of iodoform powder; mix thoroughly in sterile basin with sterilized pestle or glass rod. After thoroughly saturating the strips, wring as dry as possible, and pack the gauze strips one after another into sterilized glass jars, and seal down while moist. One strip 4½ inches wide by 4 yards long is ample for most vaginal tampons. This happens to be one-half of a square yard, that is, 3 feet by one foot and a half. A. H. Wright.]

The method of procedure for early abortion is as follows: Place the patient in the Sims position, introduce a Sims speculum, and let the assistant retract the perineum and pelvic floor (or use two fingers of one hand for such retraction, as recommended by Schauta); introduce the continuous strip of iodoformed cheesecloth, and firmly pack the vault of the vagina. In doing this one should use not the point of a sound or forceps with fine points, but something with a fairly large surface. My custom is to use the handle of a uterine sound when *packing tightly*. Continue the packing until the upper three-quarters of the vagina is filled, and then allow the end of the strip to hang out at the vulva. If in a few hours strong pains occur, indicating that regular uterine contractions are taking place, take hold of the end of the strip and pull out the material forming the plug. It may be that by this time the ovum has been separated and expelled from the uterus. If such pains do not occur remove the tampon in twenty-four hours. There will then probably be some slight dilatation of the os,

but not enough perhaps to allow the introduction of the finger. Introduce a second tampon as before. The tamponade may be kept up with safety for many days (a week or more) if the plug is renewed every twenty-four hours. It is unnecessary for the first two or three days to introduce any of the iodoformed strip inside the uterus, because the aim is to cause uterine contractions that will expel the entire ovum.

If it is found, after the removal of the second or third tampon, that the os and cervical canal are sufficiently dilated to allow the introduction of the finger, we may explore the interior of the uterus, as recommended in connection with the expectant plan, and endeavor to remove the complete ovum. If, however, a portion of the ovum has come away, the uterovaginal tamponade becomes the proper procedure.

It may be well now to repeat that the object of the vaginal tamponade is to cause the expulsion of the entire ovum during early abortion, that is, before the complete placenta is formed. The object of the uterovaginal tamponade is to empty the uterus in case of incomplete abortion (whether early or late), and also in case of late abortion, that is, after the complete placenta has been formed.

Uterovaginal Tamponade.—This procedure is divided into two stages: 1, the packing of the uterus; 2, the packing of the vagina. In packing the uterus it is generally more convenient to place the patient on her back in the lithotomy position, on a couch, on a table, or across the bed. Introduce a weight speculum, seize the anterior lip of the uterus with a volsellum forceps, and use slight traction. Or-

dinary iodoform gauze one-half to one inch wide is now pushed as far up as possible into the uterine cavity, employing a fine curved pair of uterine forceps, a uterine gauze packer, or a uterine sound to do so.

In order to carry out the second stage of the operation the patient is placed in the Sims position, and the end of the narrow strip, the greater portion of which has been passed into the uterus, is tied to the wider strip used for the vaginal tamponade. After retracting the perineum and pelvic floor, the upper three-fourths of the vagina is packed tightly in the manner previously described.

If strong uterine contractions occur the double plug and ovum may be expelled together. If no strong uterine contractions commence withdraw tampon in twenty-four hours, and introduce a new one. This procedure means, of course, that the membranes will be punctured, if they were not previously ruptured. This is suitable for all cases of abortion between the end of the third and the end of the seventh month. In the seventh month we must consider the possibility of the expulsion of a living child. In helping delivery during this month, and sometimes in the fifth or sixth month, one may introduce a gum elastic bougie (English No. 12) within the uterus or a medium-sized rectal tube (H. U. Little), as recommended by Krause, and follow with the vaginal tamponade. However, the introduction of the gauze through the cervical canal and into the lower uterine segment, with the vaginal tamponade, is generally quite sufficient to produce efficient uterine contractions.

The treatment of abortion is considered by the writer under three heads:

(1) imminent abortion may be prevented by absolute rest in bed and the use of drugs like **codeine** and **viburnum prunifolium**; (2) progressing abortion, and (3) incomplete abortion may be assisted to a spontaneous termination by a hot vaginal **antiseptic douche** and vaginal **gauze packing**. An oxytocic should be administered internally. If the result is not satisfactory after twenty-four hours, the partially dilated cervical canal should be packed with gauze and the vagina below tightly controls the bleeding, but aids in the expulsion of the placenta. He believes that the method is safe and efficacious, and prompt in its influence. Two to three drops of adrenalin solution mixed with 1 c.c. of physiological salt solution is injected. Of course, careful asepsis must be maintained. In giving the injection it is best to use a Sims speculum. If results are not prompt, the injection may be repeated in a few minutes. Grasser (Centralbl. f. Gynäk., Nu. 25, 1909).

OUTLINE OF TREATMENT IN ABORTION AND MISCARRIAGE.

	First Six Weeks of Pregnancy.		Seventh to the Thirteenth Week.		Fourth to the Sixth Month.	
	Cervix closed.	Cervix open.	Cervix closed.	Cervix open.	Cervix closed.	Cervix open.
Ovum retained.	Cervical and vaginal tamponade.	Removal with one finger.	Cervical and vaginal tamponade.	Removal with one finger.	Tamponade or dilate with small Voorhees bag.	Removal with two fingers.
Ovisac or placenta retained.	Uterine tamponade.	Removal with ovum forceps under guidance of finger.	Uterine tamponade.	Removal with one finger.	Tamponade or dilate with finger.	Removal with one or two fingers.
Placental pieces or decidua retained.	Dull curette.	Dull curette.	Dull curette.	Dull curette under guidance of finger.	Curette carefully or dilate to admit finger.	Removal with one finger.

F. J. Taussig (Surg., Gynec., and Obstet., May, 1909).

filled with the same material. Uterine contraction will thus be usually incited and everything expelled. If too much bleeding is going on, the uterus may be emptied with the finger or placenta forceps, and **ergot** administered, two or three doses usually sufficing. H. J. Boldt (Jour. Amer. Med. Assoc., Mar. 17, 1906).

Table containing the kernel of the operative indications. If conscientiously followed, it will, the writer believes, lead to considerable improvement in the practitioner's treatment of abortion and miscarriage.

For several years the writer has been in the habit of injecting **adrenalin** into the uterine cervix in cases in which there was bleeding after abortion with retention of the placenta. It not only

Conclusions based on the results in 2000 cases of miscarriage: 1. Spontaneous emptying of the uterus takes place in but about 13.2 per cent. of all miscarriages. 2. The likelihood of a miscarriage to complete itself increases with the duration of pregnancy. 3. When it becomes necessary to use artificial means to complete the miscarriage, the finger followed by the curette in later miscarriages, and the curette alone in the earlier months of pregnancy, has given uniformly satisfactory results. 4. Experience has shown that where the cervix is extremely rigid it is better to introduce the curette and break up the fetus and placenta and remove them piecemeal than to attempt to dilate the cervix sufficiently to introduce the finger. 5. Packing the vagina and lower

segment of the uterus is an unsatisfactory and often unsuccessful method of emptying the uterus. No success whatever was obtained in treating incomplete miscarriages in this way. 6. Packing is, however, of great value in two classes of cases: First, in exsanguinated patients to stop the hemorrhage and give the woman a chance to recover somewhat from the loss of blood before emptying the uterus. Second, when the cervix is very rigid, a tight cervical pack for twenty-four hours will soften it so that dilatation may be attempted with safety. 7. The results of artificial methods are as good as, but not better than, where nature has succeeded in emptying the uterus. 8. Artificial methods are necessary in a majority of cases, however, simply because nature has failed. 9. In infected cases the essential thing is to empty the uterus. 10. The later in pregnancy miscarriage occurs, the smaller the liability to become infected, but the greater the likelihood of developing grave septic complications if infection occurs. E. B. Young and J. T. Williams (Boston Med. and Surg. Jour., June 22, 1911).

In cases of hemorrhagic abortion the author has the uterine secretion examined at once, and if streptococci are found, the uterus is not evacuated but conservative treatment pursued. He does not believe the danger of fatal hemorrhage at an abortion sufficiently great to constitute a contraindication in the presence of a streptococcus infection. Neu (Münch. med. Woch., Nov. 19, 1920).

Treatment of Incomplete Abortion. —Some authors state that the uterus may be emptied at once, the cervical canal being dilated and the finger or curette or both being used. Occasionally the finger may be used with advantage when the cervical canal is well dilated, but we do not advise the use of the curette. Others hold that we should not interfere until there is decomposition of the ovum or danger-

ous hemorrhage. We do not approve of this kind of expectant treatment.

Without discussing these or other methods of treatment we recommend the **uterovaginal iodoform tamponade** for all kinds of incomplete abortion, whether occurring before or after the formation of the placenta. In these cases there is nearly always some dilatation of the cervical canal, generally enough to allow the introduction within the uterus of a narrow strip of iodoform gauze. If the canal which was once slightly dilated has again become so contracted that no gauze can be passed through it we may do the vaginal tamponade as before directed, and thereby cause sufficient dilatation for our purposes. If we use the iodoform gauze or cheesecloth instead of ordinary sterile gauze, we do not fear the danger of decomposition which is said by some to occur in the uterine cavity about the vaginal plug. If, however, one fears such an occurrence he should remove the vaginal plug in ten or twelve hours, instead of waiting twenty-four hours, as we have generally recommended. The uterovaginal tamponade may be repeated several days if considered necessary.

If after waiting one or two weeks the accoucheur has reason to fear that some portions of the egg have been retained, and there are no signs of sepsis, he may use a dull curette with great care.

In the Michael Reese Hospital from 1912 to 1914, the treatment of incomplete abortions consisted in **tent dilation** from 8 to 24 hours, **digital emptying** of the uterus when possible, otherwise **curettage,** followed by intra-uterine irrigation of ½ per cent. **iodine.** When the history and physical findings were those of an incomplete abortion, the **uterus** was **emptied**

within 24 to 36 hours after the patient entered the hospital. This was done whether or not there was any temperature. Despite the cultural findings, which in 50 cases showed the usual number of anaërobic and aërobic bacteria, the uterus was emptied in 24 to 36 hours. The value of this advice is indicated by the low mortality: .06 per cent. in 579 cases. J. E. Lackner (Surg., Gynec. and Obstet., xx, 537, 1915).

The writer gives 1 c.c. (16 minims) of pituitary extract hypodermically before curetting for incomplete abortion and finds that it produces firm uterine contraction, which makes the curettement easier and almost bloodless. H. D. Furniss (Surg., Gynec. and Obstet., Sept., 1916).

The seriousness of the retention of the ovular envelope or of placental structure has been considerably overestimated in incomplete abortion. Interference offers more risk of infection than waiting. The average physician should content himself with vaginal tamponade for hemorrhage without any intra-uterine manipulation whatever. Removal of the tampon after 12 to 24 hours is usually followed by expulsion of the retained material, though exceptionally it may be necessary to repack the vagina. If the cervix is well dilated and the ovular mass is presenting at the cervix, the latter may be expressed by external compression of the uterine fundus or withdrawn by means of a wide-blade placental forceps. Intra-uterine irrigation is condemned, and the advisability of vaginal douching is questionable. It may be necessary later, however, to dilate, curette, and pack the uterus to remove a so-called placental polyp. J. M. Fisher (Therap. Gaz., xliii, 233, 1919).

Sepsis with incomplete abortion is a very serious complication. The curette, whether dull or sharp, should never be used when there is septic endometritis or even saprophytic infection. The finger may be used very

gently to remove *débris* when the cervical canal is sufficiently dilated. Then use an intrauterine douche of warm salt solution. After the douche is used introduce iodoform gauze (the coarser, the better) into the uterus, and place a certain amount in the vagina without packing tightly. Leave this in six hours, and then remove. After this removal keep the patient as much as possible in Fowler's position, that is, a half-sitting position, to facilitate drainage. Apart from such local treatment carry out the usual line of treatment recommended for puerperal infection.

There is marked tendency among leading authorities toward conservative treatment and limiting the use of the curette. The writer found that during the 5 years, inclusive from 1910 to 1914, there were treated, in the gynecologic wards at Jefferson Hospital, 296 patients, the great majority of whom suffered from infection, many being well advanced and practically hopeless. Many of them had undergone curettement prior to entering the hospital; 127 or nearly 43 per cent., were subjected to some surgical procedure after admission. Careful analysis of the cases convinced him that a smaller mortality would have occurred had these patients been received before they had been subjected to any surgical interference and the treatment confined to non-surgical measures. It should be remembered that, even admitting the retention of embryonic products, the infective organisms do not limit themselves to the local area. If they have not already invaded the blood, the manipulation necessary to explore and remove the retained tissue breaks down the barriers nature has erected against further invasion. Montgomery (Jour. Amer. Med. Assoc., Oct. 9, 1915).

Curettage and Emptying the Uterus at a Single Sitting.—This operation

may be occasionally justifiable when there appears to be urgent need of rapid emptying of the uterus. Whether this be true or not it is recognized as a legitimate operation by some of the best obstetricians and gynecologists in the world. A brief description of the procedure is therefore given. Anesthetize the patient, place her in the lithotomy position "across bed," preferably on a Kelly pad. Prepare external parts and vagina as for vaginal hysterectomy, using especially green soap and hot water, and a hot solution of lysol or other germicide. Introduce a weight speculum, secure the anterior lip of the cervix with volsellum forceps, introduce a branched steel instrument into the cervical canal, and dilate; then introduce a curette into the interior of the uterus and scrape out its contents. Some operators then wash out the interior of the uterus with an antiseptic solution, while others use the uterine iodoform tamponade.

The advocates of the active treatment have not had as good results as those who use the expectant plan. While the latter gave a morbidity of 9.8 per cent. and a mortality of 0.8 per cent., the active treatment gave a morbidity of 29 per cent. and a mortality of 9.8 per cent. The mortality with hemolytic streptococci was 31.2 per cent. with active treatment and zero with conservative. The strictly conservative treatment is reserved for the cases showing hemolytic streptococci. W. Benthin (Monatsch. f. Geburtsh. u. Gynäk., xlii, 162, 1915).

The writer found that it was possible to empty the uterus in the early stages of pregnancy in a few minutes with the aid of pituitrin and a curette, with very little loss of blood and without shock or collapse even in the most severe cases. No hot irrigations were required to assist in the expulsion of the fetus or placenta, nor were any irrigations or packing employed after evacuation of the uterus. The injection of 1 c.c. (15 minims) of pituitrin was given after the cervix had been dilated, while the patient was under the anesthetic.

In some instances the curette was unnecessary, strong pains beginning within a few minutes and entirely expelling the uterine contents. Where the uterus was unable to evacuate itself, the curette was used to separate the adherent placenta from the uterine wall, a procedure which caused practically no bleeding, even if the placenta was removed piecemeal, owing to the firm, hard condition of the uterine wall due to the drug. The uterine cavity was wiped dry with gauze and swabbed with 5 per cent. iodine solution. It decreased in size rapidly. J. L. Bubis (Amer. Jour. of Obstet., April, 1916).

The writer recommends the following course in septic abortion: Expectant treatment is followed until the abortion is completed spontaneously. If severe or protracted slight hemorrhage makes interference unavoidable, the uterus is packed. The packing is removed after 12 to 24 hours and frequently the whole remnants of the abortion come away. If not, the packing has usually dilated the cervix sufficiently so that the uterus can be emptied manually. Repeated packing is not favored. If the uterus is not empty after the removal of the packing, it is emptied preferably by hand, if necessary after additional dilatation with Hegar's dilators and if the hand is insufficient, with the sharp curette. The longer the interval between the last rise of temperature and the operation the better. Packing afterward is avoided, unless necessitated by severe hemorrhage. The uterus is never irrigated. Ergot is given only when hemorrhage exists after complete evacuation of the uterus. Vaginal douches are never given until at least a week after the abortion and then only for subinvolu-

tion, not for purulent discharges. The patient is usually discharged 3 days after the last rise of temperature. Ries (Surg., Gynec. and Obstet., Apr., 1918).

In febrile abortion the writer prefers merely to aid the natural forces in emptying the uterus. An **ice bag** is kept constantly on the abdomen to favor uterine contractions and 0.2 Gm. (3 grains) of **quinine** given every 4 or 6 hours. In 40 to 50 per cent. of cases uterine contractions usually appear after the second dose of quinine and result in expulsion of the ovum and placenta. All lavage, irrigation, and douches are forbidden. The vulvar dressings are changed 3 or 4 times daily. Cases in which abortion cannot be effected by this method are generally left alone for 3 or 4 days, during which time the temperature usually returns to normal. **Curettage** is then performed and is easier and less dangerous, as the uterine cavity is almost empty, the uterus small, and the uterine walls firmly contracted. A. Villar (Rev. argent. de obst. y ginec., iv, 10, 1920).

Treatment of Criminal Abortion.— In the majority of cases of criminal abortion we have incomplete abortion with sepsis. We have to consider at the same time that some injury may have been done by the operator in his manipulations. One of the most common of such injuries is puncture of the uterine wall. The possibility of such injury should make us doubly careful in our methods of treatment.

Treatment of Patient with "Aborting Habit."—When we have treated a certain patient for two or three threatened abortions which have become inevitable, the presence of syphilis should be carefully inquired into. If there is a syphilitic taint, or even a suspicion of it, both patient and husband should be placed under constitutional treatment. Malformations, dis-

placements and other abnormalities of the uterus, and other conditions which act as direct causes of abortion may, of course, prevail in these cases, and should be carefully sought after.

Apart from such considerations, **rest** and **quiet** are the important elements in the treatment of such cases. The patient should be kept in bed or on a lounge from two days before the time of menstruation until three days after it ceases. In addition, if the patient is restless or sleepless, she should receive enough **opium** or other hypnotic, such as **veronal,** to make her sleep at least fairly well every night. During intervals she should have a moderate amount of **exercise in the open air,** and suitable **tonics.** Strong purgatives, vaginal douching, sports, and all kinds of fatiguing work should be carefully avoided. In case of retroversion or retroflexion, the displacement should be corrected, introducing, if necessary, a suitable **pessary,** and leaving it until about the end of the fourth month.

The automobile, particularly when used over rough roads is not infrequently a cause of abortion, especially when the fetus is sufficiently large to contribute a mechanical factor and weight to the morbid process. Horseback riding likewise increases the danger. Editors.

ABERRANT FORMS.—The recognition of such conditions obviously is of great diagnostic importance.

Missed Abortion.—The retention of the ovum within the uterus after its death is thus termed. The death of the ovum may occur before or after the formation of the placenta, but it is most apt to happen in the third month. This is probably due to the fact that at that time the egg is to some extent loosened on account of the atrophy of a large portion of the

chorionic villi. The death of the fetus frequently occurs, however, in the fourth, fifth, sixth or seventh month, and in a certain proportion of these cases the abortions are "missed."

It is a singular fact, in connection with a case of missed abortion, that the dead ovum frequently or generally remains in the uterus quiescent until term. In some cases the dead ovum still remains quiescent for an indefinite time, even after term. Although we cannot speak very definitely, we know that the dead ovum may remain in the uterus without any change in structure for one, two or more years. At least such appears to be the opinion of the majority of obstetricians at the present time.

[This fact is sometimes of great importance from a medicolegal standpoint. The case of Kitson vs. Playfair, which was tried in England about fourteen years ago, created intense interest. Dr. Playfair, the distinguished teacher and writer on obstetrics and gynecology, while treating in an ordinary professional way Mrs Kitson, the wife of Mrs. Playfair's brother, emptied the uterus, and found something like fresh placenta. Examination under the microscope confirmed his suspicion, and he expressed the opinion that there had been a recent incomplete abortion. As Mrs. Kitson had not seen her husband for over a year (he being in India and she in England) this meant a charge of immorality. Dr. Playfair informed his wife, and Mrs. Kitson was dismissed in disgrace from her ordinary circle of relatives and acquaintances. The husband in consequence entered action against Dr. Playfair. It cost the latter altogether over $50,000. Many thought also that he was not justified in revealing a professional secret. A. H. Wright.]

Mole.—When the dead ovum or a portion of it is retained in the uterus it is called by many a mole. When there has been extravasation of blood between the layers of the membranes or into the substance of the decidua, coagulation takes place and the mass with its clot or clots is called a "blood mole." When there has been repeated extravasation of blood within the ovum the blood-strata undergo partial organization and the mass is called a "flesh mole." This flesh mole retains to some extent its attachment to the uterine wall, and in some cases after partial detachment may form new attachments. Under such circumstances the detention of the mass within the uterus may be much prolonged, as before mentioned.

Treatment of Uterine Flesh Mole.—There is far from a consensus of opinion as to the treatment of such a mole. Some say leave it alone if there are not disturbing symptoms; others say empty the uterus at once when a diagnosis is made. It happens that a diagnosis is frequently difficult or impossible, and it also happens that in the majority of cases the mole is expelled from the uterus within a reasonable time. The general practitioner will be on the safe side not to interfere unless serious symptoms arise. If very serious symptoms do appear he should at once do the uterovaginal tamponade as before recommended.

Hydatiform Mole (syncytioma benignum, vesicular mole, myxoma chorii).—This is a vesicular tumor within the uterus formed by simple hyperplasia or cystic degeneration of the villi of the chorion at any time during pregnancy, but most frequently in the early months, and often after abortion.

The accoucheur, in considering the symptoms of a supposed abortion,

should ever keep in view hydatiform mole and chorion epithelioma, because early diagnosis and prompt treatment of both neoplasms are so extremely important. The first symptom of the former is a discharge of a bloody fluid which is sometimes said to resemble currant juice. Our first suspicion is generally threatened abortion. If the discharge becomes more watery in appearance, if vesicles are expelled, or if the uterus increases abnormally in size, we should suspect a vesicular mole. Generally we have to be guided by two symptoms, hemorrhage, and abnormal increase in the size of the uterus.

Treatment of Hydatiform Mole.— The condition is serious and prompt treatment is required. The uterus should be emptied as soon as possible. The following is recommended: **Dilate** the cervical canal with Hegar's dilators, then introduce a **sea-tangled tent,** then **plug** the vagina as before described. If strong uterine contractions come on within a short time remove the tampon and tent. If such contractions do not come on remove the tampon and tent in twenty-four hours, then do the **uterovaginal tamponade** as thoroughly as possible. This will, as a rule, be sufficient to cause efficient uterine contractions which will expel the mole. If there is any doubt as to such expulsion explore with the finger gently, and **scrape** the uterine wall with its tip. The metallic curette is especially dangerous in this case because the uterine walls are more or less weakened by the invasion of the cystic villi. Occasionally it may be advisable to use a dull curette, but this should be considered a misfortune, and great care should be exercised.

Chorioepithelioma (chorion epithelioma, syncytioma malignum, deciduoma malignum, choriocarcinoma). —This is a very malignant form of epithelioma developed from the epithelial layers covering the villi of the chorion. It is usually associated with abortion, and in 50 per cent. of the cases is preceded by hydatiform mole. We are told that it may occur after labor following full term, but the writer has not met such a case. Obstetricians have for some time considered that this form of epithelioma is always associated with pregnancy. Some surgeons have said recently that tumors simulating chorion epithelioma have been found not only in women in the absence of pregnancy, but also in men, and that all such have arisen in pre-existing teratomata. Obstetricians, however, do not believe that such tumors are really chorioepitheliomata. Metastatic deposits, even more malignant than the original tumor, soon appear in various parts of the body, especially in the vagina and lungs.

Hemorrhage is the earliest and most persistent symptom. The flow is at first red, but soon becomes dark and offensive. The uterus grows rapidly and is often perceptibly soft in one or more places. A hemorrhage is serious when it becomes in the slightest degree offensive. Scrapings from the uterine wall may be examined microscopically.

Treatment of Chorion Epithelioma.— A radical operation is immediately indicated. The uterus, appendages, and metastatic deposits, especially if any be found in the vagina and vulva, should be removed.

INDUCED ABORTION.—Induction of abortion is very grave in any

case, and *should never be decided on without a consultation.*

Indications.—It may be said in a general way that, in any case where the life of the patient is imperiled by the continuation of pregnancy, abortion should be induced. In nearly all cases, however, when serious disease is present it should receive prompt and careful treatment. That death of the embryo or fetus is a positive indication for the induction of abortion need scarcely be emphasized.

Tuberculosis.—It was a few years ago (and is now we fear) the custom of some physicians to induce abortion in all pregnant women suffering from tuberculosis. We have to consider, however, that in the light of our present-day knowledge tuberculosis is a curable disease in the pregnant woman as well as in the non-pregnant one. If, then, our patient has tuberculosis during pregnancy it is our duty to treat the tuberculosis and not to murder the unborn child. This should be our general rule. In a few exceptional cases (and they are very few), especially when the morbid process is far advanced, the uterus should be emptied.

Cardiac Disease.—In a large majority of women who have heart disease, pregnancy does not produce effects sufficiently serious to justify the induction of abortion. If, however, as happens in a small proportion of cases, especially when there is mitral stenosis, such symptoms as hemoptysis, precordial distress, palpitation, and great debility appear, and grow steadily worse, under appropriate treatment, the induction of abortion should be considered.

Excessive Vomiting of Pregnancy.— We have recently learned that the pernicious vomiting of pregnancy is due, in some cases at least, to peculiar disturbances of metabolism which produce a toxemia. Chemical examination of the urine shows a decrease of the amount of nitrogen excreted as urea, and an increase of the amount excreted as ammonia. In normal pregnancy, the quantity of ammonia excreted (the ammonia coefficient) is 4 to 5 per cent. In pregnancy with this form of toxemia, it may rise to 10, 20, or 40 per cent., or even higher. Williams thinks that when the ammonia coefficient exceeds 10 per cent. the pregnancy should be immediately terminated. We have found, however, that in some cases the ammonia coefficient may considerably exceed 10 per cent., and the patient may recover without the termination of pregnancy. It is hoped that further investigation will lead to conclusions which we shall all accept. We agree with Williams to some extent, however, and believe that when the ammonia coefficient reaches 10 per cent. the patient is in a dangerous condition, and needs prompt and suitable treatment. If in spite of such treatment carried out for one to two weeks she grows steadily worse, pregnancy should be terminated.

The practitioner who does not depend on this chemical test should be guided by the symptoms and condition of the patient. Indeed no one should neglect a careful study of all symptoms. It is very important that we should not wait too long. We have certainly much to learn yet respecting this very perplexing subject. We have occasionally found that the results of interference even in apparently favorable cases are sadly disappointing.

The most frequent conditions demanding induction of abortion are the toxemias of early pregnancy, pernicious nausea and vomiting, and inability to maintain the metabolism of the body. Intensive observation of these patients is required for computing the total intake and output and the total amount of nourishment retained for 24 hours. Accurate laboratory research is necessary. Heart lesions with evidence of decompensation also furnish grounds for therapeutic abortion. E. P. Davis (Therap. Gaz., xliii, 389, 1919).

General Toxemia of Pregnancy.—No definite statement can be made as to the exact time when interference is desirable in case of general toxemia of pregnancy. Apart from excessive vomiting in connection with toxemia we fear especially eclampsia. Before the onset of convulsions the induction of abortion is very rarely considered necessary. Convulsions, as a rule, do not occur in the early months of pregnancy; when they occur in the later months an immediate delivery is considered necessary. A vaginal Cæsarean section is probably safer than rapid dilatation of the cervix with quick extraction. Both operations, however, are serious, and the careful, conservative physician will prefer to resort to safer procedures. The importance of great haste in emptying the uterus has been grossly exaggerated in recent years. We think this is especially true as to eclampsia.

Chronic Nephritis. — Induction of abortion is not, as a rule, indicated in cases of chronic nephritis. Occasionally the symptoms grow so serious, in spite of suitable treatment, that the patient's life is endangered. Under such circumstances the uterus should be emptied. Disorders of vision dur-

ing pregnancy are very serious in patients who have chronic interstitial nephritis. Partial or complete blindness in such cases generally indicates a fatal termination. On the other hand, one may have absolute blindness due entirely to a state of autointoxication. In such a case the ophthalmic changes are not marked as a rule, and the sight generally returns soon after the uterus is emptied. Herringham (Brit. Med. Jour., May 7, 1910) states that this transient form of blindness is never found in uremia or associated with chronic interstitial nephritis.

Retinitis.—Affections of the eyes should be carefully studied. Retinitis should receive prompt attention. If the symptoms grow worse instead of better after treatment for a few days, interference may become necessary. In cases of retinitis with white plaques, and dimness or loss of vision, associated with serious albuminuria, abortion should be induced at once. Colin Campbell (oculist) agrees with Herringham and various modern pathologists as to the great difference between a retinitis due to an old chronic nephritis and a retinitis caused by autointoxication of pregnancy. He says the retinitis of pregnancy has a bright outlook compared with that of nephritis. Examination of the urine will materially aid a coming to an understanding of the condition. "In pre-existing nephritis the quantity is usually greater, the urea and nitrogen more nearly full normal, and the albumin and casts more abundant. In pre-eclamptic cases the uric acid and the amidoacids are markedly increased" (Can. Jour. of Med. and Surg., Oct., 1910). It may be stated in a general way that such untoward symptoms occurring early are much more serious than similar

symptoms which may appear late in pregnancy.

Pyelitis.—Pyelitis due to toxemia of pregnancy is not very uncommon, although, until recently, it was not recognized as a separate entity. Interference with pregnancy is not generally required. If, however, the temperature keeps above normal for four weeks; if there is much pus in the urine; if the leucocyte count is high, abortion should be induced. It is better if possible, however, to defer interference until the child has become viable.

Ante-partum Hemorrhages.—Hemorrhage from placenta prævia is our chief concern in this connection. If interference becomes necessary we should employ the **vaginal tamponade,** and should never dilate the cervix to the slightest degree. If the hemorrhage is increased by complete- or partial separation of a placenta normally situated the same rule as to treatment applies. Such hemorrhages do not occur frequently before the child is viable, and, consequently, need not be discussed in detail here.

Retroflexion of the Uterus.—When serious symptoms appear because of retroflexion or retroversion of the uterus, and the misplacement cannot be corrected, it may become necessary to interfere. In the majority of such cases abortion takes place without any interference.

Contracted Pelvis.—The induction of abortion in cases of contracted pelvis was for a long time considered indicated. We hope it is generally conceded now that such a procedure is both incorrect and sinful. We have learned in recent years that conservative **Cæsarean section,** done at the proper time with reasonable care and skill, is one of the safest and best operations now known to surgery. Such having been demonstrated, we have done well in ceasing to destroy unborn children because of contracted pelvis.

Hydramnios.—When the hydramnios causes the distention which seriously affects the mother's health we may have to consider the desirability of emptying the uterus. In such cases, however, we can generally wait until the child becomes viable.

Appendicitis, Ovarian Tumor, and Other Abdominal Growths.—Abortion should not be induced for any of these conditions. The ordinary operation for the disease or new growth should be performed.

Goiter.—As a rule there should be no interference, at least until the child is viable.

Myoma Uteri.—No interference with pregnancy is indicated as a rule. In a limited proportion of cases one or more fibroids may be so situated that delivery in the ordinary way is a physical impossibility; but, even under such circumstances, the induction of abortion is very rarely indicated. We may, however, meet a uterus in which the growth would interfere with normal delivery, but in this case the child might be delivered by Cæsarean section if pregnancy went on to term. Women with very bad fibroids seldom conceive, and when they do early abortion is apt to occur.

Chorea.—In a certain proportion of severe cases of chorea the patient goes from bad to worse, notwithstanding suitable treatment. In very serious cases the woman grows worse very rapidly and dies unless the uterus is emptied. In many cases this serious procedure, unfortunately, does not save the patient.

In many cases pernicious anemia in pregnancy seems to be due entirely to the pregnancy. When untreated, it usually results in premature labor, fetal death, or death of the mother. In metaplastic anemia developing during the first 3 months, abortion should be induced at once. Later, especially when hypoplastic, the patient should be treated medically at first, and pregnancy interrupted later. A. Frers (Rev. argent. de obst. y ginec., iii, 430, 1919).

Method of Inducing Abortion.—For the induction of abortion we employ the methods and procedures generally used
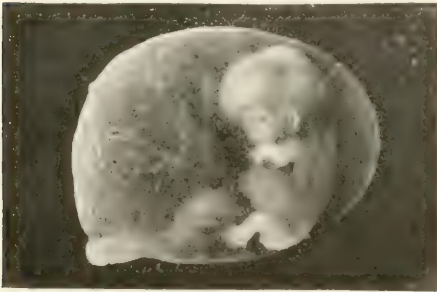
Amnionic sac containing embryo and waters. The thick decidua retained in uterus. (Seven weeks.)

in cases of inevitable abortion (which see). When speaking about the treatment of the latter we had in view the fact that nature, chiefly through uterine contractions, and hemorrhages, had done something, perhaps much, in the process of abortion. The ovum has been more or less loosened from its attachments, and the cervix has perhaps been more or less dilated. In considering the induction of abortion, we assume, on the other hand, that the ovum is pretty firmly attached to its moorings, and that the cervical canal is not dilated. Under such circumstances it is more difficult to empty the uterus. The following recommendations are made for the induction of abortion at different

periods of pregnancy up to the seventh month. This course seems advisable, although it will mean a certain amount of repetition:—

In any case prepare the patient as for vaginal hysterectomy, or as has been for curettage, previously described.

Pregnancy, three months, showing fetus below. Placenta formed.

First or Second Month.—Introduce a vaginal tampon of iodoform cheesecloth as before described. This may be removed, and reintroduced, every twenty-four hours for five or six days. In many cases these vaginal tampons will not produce the desired result, even in five or six days. Under such circumstances one may introduce a narrow strip of iodoform gauze within the uterus after the first or second day. If, in doing this, one punctures the mem-

brane, no serious harm will be done. After such introduction, practise vaginal tamponade. It may be necessary to do more than the introduction of the gauze; if so, adopt the old-fashioned method of introducing a uterine sound, and purposely puncture the membranes if possible. This is suitable, especially in cases of pernicious vomiting, because such puncture allows the escape of the liquor amnii, and such escape often causes the serious symptoms to subside immediately. It happens that in certain cases it is difficult to puncture the membranes because the deciduum is thick, tough and elastic.

Third Month. — Carry out the methods recommended for the first and second months. There is less chance of causing the expulsion of the entire ovum and on that account it is not well to wait long before invading the interior of the uterus.

Fourth and Fifth Months.—Practise a uterovaginal tamponade as before described as rapidly and thoroughly as possible.

Sixth and Seventh Months.—Introduce a vaginal tampon, remove in twenty-four hours, place patient in lithotomy "across bed" position: introduce a weight speculum, seize the anterior lip of the cervix, pass a gum-elastic or hard-rubber bougie, or a medium-sized rectal tube within the uterus, between the membranes and uterine wall to the fundus if possible. Then place woman in Sims's position, and plug vault of the vagina tightly. Labor will generally come on in a few hours, and the uterine contents will soon be expelled. It is sometimes advisable to introduce the bougie in the fifth month.

We find that in some cases the tamponades are not efficient, and we are compelled to adopt more forceful procedures. As before mentioned we think the use of the metallic dilator and sharp curette in the "single sitting" operation is always dangerous. If this statement is true, or even half-true, it is sad to notice that some of our ablest authors in recent textbooks say that "the induction of abortion is practically free from danger if perfect asepsis is observed." This operation is especially dangerous in the class of cases included in this chapter because the patient is generally in a bad physical condition from the complication which calls for the termination of pregnancy, as, for instance, pernicious vomiting.

It is generally an easy matter, especially after a vaginal tampon has been in place twenty-four hours, to dilate the cervix with the Hegar dilators sufficiently to allow the introduction of the gauze within the uterine cavity. We also recommended the use of the laminaria (sea-tangle) tent for dilatation. It is said, however, that there is great danger of infection from the use of any tent for such purpose. There was, of course, much reason for such fear many years ago when the sponge, tupelo and laminaria tents were not sterile, and, in addition, were not used in an aseptic way; but during recent years we have been able to get excellent sterile laminaria tents that are perfectly safe if used in a cleanly way.

Similar objections have been raised against tampons because they also were unsafe as used many years ago, but the tampon medicated with iodoform or other suitable antiseptic is as safe as anything that can be introduced within the uterine cavity. It is thought by some that there is danger from the use of the bougie according to Krause's method, but, if the bougie is made per-

fectly sterile by boiling and is carefully used, the danger therefrom is very slight. It is well to remember, however, that there is always some danger in connection with any obstetrical operation through want of care on our part. We should ever make a continuous effort to guard against such danger.

<div align="right">A. H. WRIGHT,
Toronto.</div>

ABORTION, TUBAL.—

DEFINITION.—Early interruption, *i.e.*, abortion, is the natural outcome of extra-uterine pregnancy, whether by reasons of insufficient blood-supply or unfavorable mechanical conditions for the continued development of the fetus.

[A brief review of the history of this important subject ought to possess for us more than ordinary interest because of the important rôle played in its development by one almost of our own number and generation in whom we may take a pardonable local pride. I refer to the illustrious and lamented John S. Parry. He was not the first to write upon the subject. Indeed, Albucasis, the Arabian, in the eleventh century recognized and described a case of extra-uterine pregnancy. Nor was he the first to grasp the possibilities of operative treatment in the emergency of rupture. That was proposed by Harbert, of New York, in 1849. The merit of Parry consisted not only in grasping the significance of the catastrophe and the correct mode of meeting the emergency, but in applying his philosophical mind and scholarly attainments to the production of a monograph which by its masterly marshaling of facts and lucidity of deduction should have quieted the doubts of Thomas. He was able to collect for his book, which was published in 1876, 500 cases reported in the literature. Of 499, in which the result was stated, 366 died and 163 recovered. Of the deaths, 174 had been from rupture. Of these deaths 81 had died within 24 hours. These figures were his text. He began his sermon with this sentence: "From the middle of the

eleventh century, when Albucasis described the first known case of extra-uterine pregnancy, men have doubtless watched the life ebb rapidly from the pale victim of this accident, but have never raised a hand to help her." Then, though not himself a surgeon, he points out the plain surgical indications. In the same year as the publication of his monograph he died, doubtless depriving the world of one who was destined to become one of its greatest figures in the advancement of medicine. Parry was a pupil of my father, who often used to speak of his studious habits and scholarly grasp. He was by nature fitted for mental leadership.

The honor of performing the first operation for this emergency went to Lawson Tait in 1883. He had been earnestly solicited to operate for this condition in 1881 by a physician who had correctly diagnosed a case of rupture with internal hemorrhage. He refused, and the patient died shortly after. Unfortunately the first patient operated on died also, but his change of heart was complete, and, correctly attributing his failure in the first case to faulty technique, he altered his method and continued to operate all such cases. Of the next 40 cases only 1 died. Truly a brilliant record which was not long in converting the medical fraternity.

The original microscopical preparations of Tait in which he demonstrated his ideas on extra-uterine pregnancy and pelvic hematocele which, before him, were in a very confused state are still to be seen in the museum of the Royal College of Physicians in London.

There are many other names of more or less importance in connection with the development of the subject, but these two are central and all we have space to consider. JOHN B. DEAVER.]

SYMPTOMS.—The symptoms of extra-uterine pregnancy include those due solely to the condition of pregnancy and those which arise only from its abnormal situation. Inasmuch as the majority of cases terminate within three months, at which ordinary signs of pregnancy are not usually pronounced, we do not often get much help from the symptoms belonging to the first group. Yet

such symptoms and signs as enlarge-
ment of the breasts, the presence of
colostrum, cessation of menstruation,
increased vascularity of the genitalia,
softening of the cervix and body of
the uterus with slight enlargement,
disturbances of the bowels or bladder,
morning nausea, and the abnormal
appetite, cravings or sensations which
the multipara sometimes recognizes,
are occasionally of confirmatory value.

It would be desirable to make the
diagnosis before rupture were it pos-
sible to do so. Unfortunately a large
percentage of cases give such trifling
evidence of the true condition, if
indeed there be any prodromal symp-
toms at all, that no suspicion is
aroused. Still it is occasionally pos-
sible to make the diagnosis and it
should be our effort to do so. One
operator, Baldwin, of Columbus,
Ohio, has reported 11 such cases.

Lejars holds that a prolonged continu-
ous blood-stained uterine discharge is an
important aid in differentiating tubal abor-
tion; even if the proportion of blood is
small its persistence for two up to five
weeks is characteristic, and absence of
blood in the vaginal discharge is strong
evidence against a recent hematocele. The
slight hemorrhage seems to persist longer
after tubal abortion than after rupture.
Incomplete expulsion of the ovum is also
liable to keep up the hemorrhagic dis-
charge, and the writer relates some in-
stances of such retention of the placenta
with the tube open and of total retention
with the tube closed. The small encap-
sulated collection of blood may be taken
for a fibroma, and the resulting disturb-
ances for inflammatory processes in the
adnexa or in the uterus. Certain cases of
tubal abortion have been diagnosed as a
hemorrhagic metritis, and the uterus was
curetted when this organ was sound and
the trouble was in the tube beyond the
reach of the curette.

According to Holden a sign of tubal
pregnancy is a more or less striking pale-

ness of the cervix. The absence of this
paleness does not, however, exclude this
condition, but its presence, when not due
to obvious other causes, is almost pathog-
nomonic. It is only present, however, in
those cases in which there is bleeding
from the uterus. EDITORS.

The diagnosis in these cases rests
upon: first, a consideration of the his-
tory. Important points for considera-
tion are the age of the patient,
exposure to pregnancy and the pre-
sumptive signs and symptoms, a
history indicative of an antecedent
tubal inflammation, a previous period
of sterility usually of some years.
This last point has been observed by
all students of the condition and
Parry remarks on what he calls "the
previous inaptitude for conception"
of these patients.

Amenorrhea of shorter or longer
duration is a fairly constant feature
and is followed in the majority of
instances by irregular bleeding from
the uterus, sometimes profuse, some-
times a mere staining. The history
of passing bits of tissue or the demon-
stration of decidua in the discharge
is important.

Pain if felt before rupture consists
frequently in vague uneasy sensa-
tions in the pelvis. Sometimes it is
more severe, colicky in type and ac-
companied by nausea.

In cases which show any of these
suspicious symptoms an internal ex-
amination should not be neglected.
The demonstration of a pelvic mass
lying outside of the uterus, in the
presence of a probable pregnancy, is
a very suspicious circumstance. If
this mass should correspond in size
with the duration of pregnancy, if it
should be located in the course of
the tube, if it be movable, moderately
soft and very tender, we may fairly

conclude we are dealing with a case of extra-uterine pregnancy. It must be remembered that it is sometimes easy to mistake a retroflexed pregnant uterus for an extra-uterine pregnancy.

A study of 36 cases simulating tubal pregnancy by Crossen showed that the following conditions may be mistaken for it: 1, an acute exacerbation of a dormant gonorrheal pyosalpinx; 2, sudden extension of a uterine gonorrhea to the tubes and peritoneum; 3, an early abortion if associated with salpingitis or a tumor; 4, an irregularly softened, misplaced, hyperesthetic uterus associated with tubal enlargement; 5, an unsuspected tumor associated with symptoms of early pregnancy; 6, ovarian hemorrhage or tubal hemorrhage from other conditions; 7, sudden and rapidly progressive salpingitis, appendicitis, and gastrointestinal perforations.

A positive diagnosis of unruptured ectopic pregnancy or tubal abortion should be made in the vast majority of cases. In his service at the Long Island College Hospital, and in over 250 personal cases, a positive diagnosis was made in over 85 per cent. of the cases. This is due to the fact that a very careful history was taken and a thorough physical examination made in each instance. The conditions, pathological or mechanical, that may cause a delay in the progress of the impregnated ovum are always indicated in the history if the attending physician or surgeon takes the trouble to correlate the facts as stated by the patient. The diagnosis of ruptured ectopic with the consequent hemorrhage and shock is obviously very much easier to diagnosticate. J. O. Polak (L. I. Med. Jour., xii, 121, 1918).

Often before a diagnosis *can* be made, usually before the diagnosis *is* made rupture of the tube or extensive separation and hemorrhage from the placental site supervenes. It was formerly thought that rupture was the most common outcome of tubal pregnancy. More careful examination of the specimens, however, has shown us that in many cases of supposed rupture we are dealing with a case of tubal abortion with hemorrhage from the site of implantation. Moreover, hemorrhage from this source, while less violent as a rule than in rupture, may be very severe and even fatal. Frequently, however, it is comparatively slow and by slow leakage is responsible for the majority of hematoceles which we find. Recent statistics indicate that these tubal abortions occur more frequently than does rupture. The tragic stage, however, may follow either process.

[The idea that rupture is not so frequent as has been supposed and therefore an extra-uterine pregnancy is not so dangerous a condition is fallacious. It is a matter of common knowledge that tubal abortion may give rise to a condition as serious as any of the accidents of ectopic pregnancy. I should not feel it necessary to insist on this fact were it not for an impression which is going abroad in regard to treatment, which I shall consider later. JOHN B. DEAVER.]

There are instances in which a strong presumptive diagnosis can be made and for lack of which the patient suffers. There is usually a cessation of menstruation for one or more periods, and in this case, with rupture threatening, it is usually reestablished, irregular as to time, and of a tarry, sticky character which, according to some observers, is pathognomonic. The pain is usually cramplike, occurring at intervals for several days, and following it there is a dark, sanguineous discharge, probably due to a partial rupture of the gestation sac. Microscopic examination will reveal traces of decidua in most cases. A careful and thorough examination is advisable and great care should be employed to avoid rupturing the sac. L. G. Bowers (Jour. Amer. Med. Assoc., Feb. 12, 1910).

Pain is a very important symptom. It is sudden and acute in its onset; is located in the affected tube; is distinct but rarely very severe prior to rupture (Zinke); and the attacks soon pass off. It is generally sickening in character, and it is usually the one symptom which induces the patient to visit her physician. The tubal cramps result from an attempt on the part of the tube to expel the ovum or the blood which has exuded into its caliber. Considerable blood may escape through the fimbriated extremity in this way, causing slight localized peritonitic attacks with resultant adhesions. The history of colicky attacks may cover several weeks before the final rupture of the sac. A vaginal exploration shows an exquisitely sensitive mass lying in close juxtaposition to the uterus, a strongly presumptive diagnosis of the condition may be made. The enlarged tube can readily be palpated bimanually in most cases, unless the abdominal wall is very rigid or unduly thick. Such a tumor is unilateral, in distinction from inflammatory and purulent affections of the tubes, and while partially fixed it is not firmly adherent, presenting a board-like rigidity, as in the case of a pus-tube. It can be readily felt through the vaginal vault, and is commonly the seat of distinct arterial pulsation—another feature which is generally absent from inflammatory conditions of the tube. Dorland (Jour. Kans. Med. Soc., Nov., 1915).

Of the 75 cases of bilateral tubal gestation reported in the literature, about 41 may be considered as simultaneous gestations. But 8 of these cases are doubtful, reducing the figure to 33 cases. Practically the diagnosis of bilateral pregnancy is never made before intervention. On intervening for a tubal pregnancy, the annex on the opposite side should always be examined. If a hematosalpinx is found it must always be removed. Proust and Buquet (Rev. de gynéc. et de chir. abd., xxiii, 353, 1916).

Abdominal pain was present in all cases, varying from the classical crisis with the following shock from hemorrhage to the more or less continued abdominal distress, which brought the 36 patients for examination to the writer. The former condition with its clearcut evidence of intraperitoneal hemorrhage is not usually mistaken, but the slow process with its distress from tubal distention or slight rupture is very confusing. In a case of irregular bleeding and abdominal pain, one must have constantly in mind 3 conditions, namely, intra-uterine pregnancy with threatened abortion; inflammatory tubal disease, especially hydrosalpinx and pyosalpinx, and extra-uterine pregnancy. C. B. Lewis (Jour. Amer. Med. Assoc., Sept. 21, 1918).

In 183 cases of ectopic pregnancy sudden onset of abdominal pain occurred in less than half of the cases, colicky pains in the lower abdomen in a little more than one-third, and abdominal tenderness in four-fifths. Vaginal examination showed the uterus enlarged in nearly one-third, and a palpable mass, which was usually tender, was found in one of the fornices or the cul-de-sac in over two-thirds. The temperature on admission was above 99 degrees in nearly three-fifths of the cases. Fever was more frequent and rose higher in those in which the internal hemorrhage was greatest.

The most frequent error in diagnosis was acute or chronic tubal infection, and the next, abortion and acute appendicitis. Usually a careful history and physical examination will lead to a correct diagnosis in unruptured cases. H. F. Lewis (Ills. Med. Jour., xxxvii, 301, 1920).

Rupture is the most serious accident of ectopic gestation. It may take place very early and be the first symptom. Cases have been reported of rupture in the first or second weeks of pregnancy. Usually it occurs in the second or third months, but occa-

sionally may be delayed into the later months. Secondary rupture may occur at any time after primary rupture up to term. Rupture is usually ushered in by severe lancinating pain in the hypogastrium, accompanied by shock, sometimes by syncope and frequently by nausea or vomiting.

of the abdomen which is readily distinguished from the usual rigidity of inflammation of the peritoneum.

There are the symptoms of rupture and of hemorrhage *per se*. They are not always so frank and outspoken and in order to be sure of our ground it is frequently necessary to bring to

DIFFERENTIAL DIAGNOSIS BETWEEN EXTRA-UTERINE PREGNANCY AND EARLY ABORTION BASED ON A CAREFUL STUDY OF 28 CASES.

EXTRA-UTERINE PREGNANCY.	EARLY ABORTION IN UTERINE PREGNANCY.
1. Advent is sudden.	Rarely sudden.
2. Pain is severe very early.	Not severe early.
3. Blanching of the face early.	Blanching of the face late, if ever.
4. Pulse very feeble and rapid early.	Pulse strong and full until late.
5. Hemorrhage usually not severe, but persists, even after the uterus has been thoroughly emptied.	Hemorrhage usually severe early and markedly, diminishes after the uterus is emptied and ceases entirely in a few days.
6. At first there is no elevation of temperature, and later it is rarely above 101° F.	Frequently, especially if there is sepsis, the temperature is very much elevated.
7. At one side of the uterus there is usually a very tender tumor, which is, as a rule, movable.	There is no tumor unless there is infection, and then it is rarely movable.
8. Boggy feeling behind the uterus.	Not present.
9. Usually the cervix is very slightly open.	It is open, especially if part of the products of conception are still in the uterus.
10. Shreds, decidual membrane and blood only escape.	An embryo may be found; if not, the microscope will show chorionic villi.
11. Late there will be marked diminution of the hemoglobin (30 per cent. to 70 per cent.).	No marked diminution of hemoglobin.
12. Rarely, if ever, polynuclear leucocytes.	Frequently present, especially if there is infection.
13. If the *cul-de-sac* of Douglas is opened, blood will escape with possibly an embryo.	No blood will escape.

Ralph Waldo (Archives of Diag., Oct., 1908).

Following this the symptoms of internal hemorrhages make their appearance. Increasing pallor, rapid and weak pulse, sighing and labored respiration and air hunger, dimming of vision, with increasing but slight distention of the abdomen, signs of fluid in the flanks, general abdominal tenderness most marked in the hypogastrium and a peculiar doughy feel

our aid the history and the internal examination. In this condition as in so many others, the classical picture *in toto* is rarely seen and it has happened, paradoxically enough, as Douglas remarks, that many more diagnoses are made nowadays since the integrity of all the classical symptoms have been repeatedly attacked than when a clear average picture had

been drawn and accepted. It will do then to know that the three cardinal symptoms are pain, menstrual irregularities and tumor if we appreciate their variability.

Conclusions based on a study of 214 cases: 1. Irregular flowing seems to play the important part given it in the books as a symptom of extra-uterine pregnancy. 2. The importance of a long period of sterility as a cause of extra-uterine pregnancy does not seem to be borne out by these statistics. 3. Conditions possibly leading to extra-uterine pregnancy: The fact that cystic ovaries, disease of the opposite tube, adhesions, or a previous miscarriage occurred in over 83 per cent. of 202 cases is suggestive, and is in agreement with authorities as to the possible relation of such conditions to extra-uterine pregnancy. 4. The fact that in only 26.5 per cent. of 207 cases the pain was sudden is of interest. In about three-fourths of the cases the sudden severe pain was preceded by pain of less severity, coming on gradually. 5. Of considerable interest is the leucocytosis observed in the cases in shock. This is apparently a perfect example of leucocytosis after hemorrhage. The finding of a temperature of 100° or over in 43.4 per cent. of the cases, and of a temperature of 101° or over in 14.4 per cent. of cases, is also of interest. Ordinarily it is supposed these cases rarely have any fever. Coues (Boston Med. and Surg. Jour., May 11, 1911).

[The question of great and timely interest in connection with the treatment of extra-uterine pregnancy has to do with the management of the case at the time of rupture, with associated hemorrhage and shock. Thanks to the early operation these complications are rare nowadays, but I fear, if the advocates of delayed treatment secure a following in the profession, that these cases may occur more frequently, and that cases which would be noted in the statistics of extreme conservatives as cures will later succumb to a condition which is the direct result of the Fabian policy. John B. Deaver.]

COMPLICATIONS.—I have already pointed out that spontaneous cures may occur without leaving a dangerous condition behind and have remarked on the rarity of such a favorable outcome. More usual is it for a collection of blood, often very large, to be left as a foreign body in the peritoneum.

These collections or hematoceles excite a reactive peritonitis which serves to glue together the intestines and encapsulate the mass of clots. Absorption and organization of such a clot may take place, but is usually very slow. In the mean time not infrequently infection occurs. The danger of this is apparent when we realize that an hematocele is nothing but a most inviting medium for bacterial growth, situated about the rectum or lower bowel, which harbors the most virulent bacteria.

[An infected hematocele is a serious condition and demands prompt evacuation and drainage. This is best done by way of the vagina, if possible. At times it is necessary to attack it by the abdominal route, accepting the danger of a subsequent peritonitis. John B. Deaver.]

Obstruction of the bowel is mentioned by Parry as the cause of death in a number of instances. The mechanism of this is by the peritoneal adhesions set up by the old extravasation of blood or a degenerated fetus in neglected cases.

Case of extra-uterine gestation sac which ruptured into the large intestine. A five-months fetus with cord and placenta was passed from the rectum, and the patient recovered. Martin (Münch. med. Woch., Aug. 21, 1906).

A pregnancy which is allowed after rupture to develop free in the abdomen or in the broad ligament later furnishes a very difficult problem to

the surgeon owing to the danger in dealing with the placental site, and the mortality in such cases is much higher than in the early cases. Left entirely to itself the fetus often becomes infected, and the earliest records we have of extra-uterine pregnancies are of cases in which this occurred, the resulting abscess later spontaneously discharging through the abdominal walls, when its nature was surmised by the appearance of degenerated fetal parts in the discharge. Sepsis, exhaustion and death were noted in 54 of Parry's cases.

A new sign in ruptured extra-uterine pregnancy was identified by the writer. The patient, a woman of 38 years of age, suddenly developed abdominal pain and distention. Three weeks later, *the umbilical region was bluish black,* although she gave no history of injury. On opening the abdomen the writer found a right-sided extra-uterine pregnancy, and about 1½ quarts of free blood in the abdomen. A case is reported by Ransohoff, where a man, 53 years of age, in whom at operation rupture of the common duct revealed much free bile in the abdomen. As he showed a similar discolored area the writer concluded that the bluish black appearance of the umbilicus in his own case was due to intra-abdominal hemorrhage, and the presence of the nodule to the side of the uterus established the diagnosis of extra-uterine pregnancy. T. S. Cullen (Trans. Amer. Gynec. Soc.; N. Y. Med. Jour., Aug. 17, 1918).

ETIOLOGY AND PATHOGENESIS.—In attempting to get a clear idea concerning the causation of extra-uterine pregnancy, one is quite awed and overcome by the vast number of hypotheses which have been advanced to account for this curious anomaly.

[It is not surprising that there is still much obscurity in the etiology. A correct understanding of the pathology of any condition presupposes a fairly exact knowledge of the normal physiology of the parts. There still exist many problems connected with maturation, ovulation, impregnation, implantation and development. Some of these problems carry us well back into the shadowy realms of the beginnings of life itself, that ultima Thule of the biologist.

The incompleteness of our information concerning these abstruse secrets of nature forces us here, as in so many other medical problems, to resort to the methods of induction and experience, and if we have not yet arrived at the point where we may safely take the inductive hazard it is because we may not yet have appreciated fully the saying of old Ambroise Paré that "such matters cannot be determined by sitting down and thinking, but by hard unremitting toil."

Gradually, however, our knowledge of the normal functions of procreation has been expanding and a sufficient number of cases have been observed, recorded and analyzed to enable us to recognize certain factors which evidently play an important part in the etiology. JOHN B. DEAVER.]

Lawson Tait originally thought that the ciliary current of the mucous membrane of the tubes and that of the uterus was in opposite directions, that of the tubes being directed toward the uterus and that of the uterus moving upward, thus forming a natural meeting place of sperm and ovum at the fundus. He considered it abnormal for spermatozoa to gain an entrance into the tubes and held that impregnation occurring in the tubes through this accidental invasion of the spermatozoön was very likely to give rise to tubal pregnancy. This beautifully simple conception has yielded to the iconoclastic power of observed facts. We now know that the ciliary current of the uterus as well as that in the tubes is downward. We know that the spermatozoa can

readily stem this current, their rate of speed being calculated by Henle as 1 cm. in three minutes.

We know that they quite regularly obtain entrance into the tubes and swarm up its lumen and it seems quite probable, if not certain, that impregnation in the tube is common, if not the regular method. Once fertilization has taken place development begins at once. The ovum, comparable in many respects to a parasite, rapidly throws out the chorionic villi which lay hold on the maternal tissues and by erosion secure anchorage and open up the intervillous blood spaces. Just how soon the ovum displays these grasping tendencies is unknown. The youngest ovum of which we know was discovered by Peters in the uterus of a woman who committed suicide three days after missing her period. It measured .6 x .8 x 1.3 millimeters and was firmly implanted with numerous projecting villi in the process of formation. Certainly this ovum was less than a week old. Just what condition must be met by the maternal tissues to permit of implantation is uncertain. Webster is quite certain that there must be a decidual reaction and a number of observers have reported having seen decidual formation in the tubes.

Normally the oösperm is swept down into the uterus before it effects a lodgment. The forces which accomplish this movement are the peristalsis of the tube and the action of the cilia. Whatever delays the ovum in transit, permitting it to put out the anchoring villi, in the presence of a suitable soil, renders imminent the occurrence of an extra-uterine gestation.

Analyzing 309 cases, the writer found that infection or mechanical alteration due to adhesions of the Fallopian tube predisposes to ectopic gestation. The onset of symptoms occurs as frequently at the time of an expected period or just after a normal period as it does when a period is overdue. Pain, with or without bleeding, was present in every case, unless unruptured. L. K. P. Farrar (Amer. Jour. of Obstet., June, 1919).

As to the nature of the soil required by the ovum we are not so certain. Concerning the influence of delay which is governed by mechanical causes everyone is agreed.

These causes may be classified as:—

1. Malformation: as diverticula, accessory ostia, and persistence of the greatly convoluted fetal contour of the tubes.

2. Obstruction from within: as in tubal polypi and torsion of the tube.

3. Obstruction from without: as in myoma and peritoneal bands and adhesions.

4. Inflammation, which acts by destroying the motor power of cilia and musculature and secondarily by the formation of different types of obstruction.

5. Excessive size of the ovum itself, as in the delay which occurs in external migration of the ovum.

The importance of the inflammatory factor in the etiology of ectopic gestation is becoming more and more appreciated and is even of use in the diagnosis, a history indicating more or less pronounced salpingitis tending to arouse our suspicions of the greater possibility of an extra-uterine pregnancy in a doubtful case.

An analysis of 170 cases in the author's clinic showed that tubal pregnancy sometimes results from an infan-

tile condition of spiral torsion of the tubes, but chiefly from residues of old gonorrheal or inflammatory puerperal processes. In the diagnosis inflammatory conditions may be differentiated from ectopic gestation by the leucocyte count and by puncture of the posterior vaginal wall. Fehling (Arch. f. Gynäk., Bd. 92, Hft. 1, 1911).

According to the site of implantation we recognize several varieties :—

1. The interstitial, located in that part of the tube which pierces the uterine wall.

2. The isthmial.

3. The ampullar.

4. The infundibular.

5. The ovarian.

These are the primary forms. Later the gestation sac by reason of rupture or growth may change its position, giving rise to the secondary forms.

Thus the interstitial form may be converted into an intra-uterine by rupture into the cavity of the uterus, into an abdominal by rupture into the general cavity or into an intraligamentary by escape between the layers of the broad ligament. The isthmial and ampullar forms similarly may become tuboabdominal, tubo-ovarian, abdominal or intraligamentary. An infundibular or ovarian pregnancy always tends to become abdominal. The last-named condition is one of the greatest curiosities of abdominal pathology. All the undoubted cases of ovarian pregnancy so far observed can be numbered on the fingers. The interstitial and infundibular forms are almost as great rarities; so that for practical purposes we have to do only with cases primarily isthmial or ampullar, of which the latter are most numerous, and with the forms secondary to these primary varieties.

Extra-uterine pregnancy assumes pathological significance when it undergoes ectopic attachment. The tubal ovum has a parasitic action, malignant in that it destroys maternal tissues; it embeds itself in the tube wall, and tends to the death of the mother. The growth of the ovum or the enlargement of the dead ovum mass, thinning and destroying the tube wall, leads to almost certain rupture of the tube. Primary rupture may be partial or complete and fatal. If incomplete, subsequent ruptures will be almost certain to follow. With rupture free hemorrhage occurs, which may prove fatal. There may be one rapid fatal hemorrhage or a series of minor hemorrhages. If death does not occur from hemorrhage, the blood and the ovum in the abdominal cavity may act as imitating foreign substances which lead to loss of function and pathological changes in the viscera, to local or general infection, thrombosis, embolism, etc. The dead ovum is almost as harmful as the living one, from the standpoint of rupture, and may be more harmful as a focus of infection. C. W. Barrett (Amer. Jour. of Obstet., June, 1911).

Report of a case in which the ovary was removed on account of supposed cystic enlargement. A fetus was found in it, the ovarian elements having nearly all been superseded by the intact developing ovum. W. Liebe (Monats. f. Geb. u. Gynäk., Feb., 1921).

The natural outcome of extra-uterine pregnancy, as stated in the definition, is early interruption, whether by reasons of insufficient blood supply or unfavorable mechanical conditions for the continued development of the fetus.

The most common event is the formation of a tubal mole from the slow leakage of blood about the sac. This soon results in the death of the fetus and cessation of growth. In this way spontaneous recovery may

occur. I have several times in the course of pelvic operations encountered old tubal hematomata which were clearly the result of a previous tubal pregnancy which had terminated itself and retrogressed without giving the patient any great inconvenience. That this is not a frequent occurrence our clinical experience and the infrequency of such operative findings testify. There is evidence to show that even after the death of the fetus the chorionic villi may continue to grow and exert an erosive action on the wall of the tube which, coupled with the distention due to hemorrhage, may bring about a rupture. More common than this is the gradual extrusion of the mole from the fimbriated extremity, a process known as tubal abortion. Rupture of the tube and tubal abortion may take place rapidly without the previous formation of a mole. These are apt to be the fulminating cases.

Hemorrhage is more free in case of rupture than in abortion as a rule: more free in rupture into the general abdominal cavity than in rupture into the broad ligament, more free when the site of rupture involves the placental attachment, and more free at the cornual end of the tube than at the ampullar end.

[This latter tendency was tersely expressed by Formad, who used to say, "Ruptured cornual cases belong to the coroner; ruptured ampullar to the surgeon." Surgery in its march has modified this statement, but it still serves to point out the relative dangers. JOHN B. DEAVER.]

Hemorrhage is the outcome of extra-uterine pregnancy which chiefly concerns us from a practical standpoint. It is probable that no case of ectopic gestation occurs which is not accompanied by hemorrhage at some time. It may, however, be early or late, slow or rapid, slight in amount or profuse. It is the chief, though not the only, factor in the production of so-called shock, and is the main agent in a fatal outcome. I shall have more to say concerning hemorrhage under the question of treatment.

If the patient be fortunate enough to survive the primary rupture and the fetus live, she still has to face the possibility of a second rupture of the gestation sac in its new position. Occasionally an extra-uterine pregnancy may progress to term. Usually this is rendered possible by the escape of the fetus within its amniotic sac into the general abdominal cavity, the placenta remaining attached at the primary site. In this event, after a spurious labor at term, the fetus dies and offers an inviting site for infection.

[Operation is here indicated on the same principle as in the case of any foreign body which threatens the host. This holds true in spite of the well-known fact that in some instances the fetus has caused little harm, being converted into a lithopedion or adipocere. Such a late terminal event presupposes a series of diagnostic failures which we trust, now that the condition is so well known and understood, may not come to pass. JOHN B. DEAVER.]

TREATMENT.—This involves a discussion of the immediate considerations concerning an active *versus* expectant mode of treatment in cases of rupture.

[It has long been my practice to operate every acute case of extra-uterine pregnancy without delay and my results have been so uniformly good that it would never have occurred to me to reopen the question. Robb, in 1907, came forward with the as-

sertion that surgeons were losing many of their desperate cases from overhaste in operating during shock. He believes that shock is mainly due to the effect of the accident of rupture upon the nervous system, that it would be a great rarity for a patient to bleed to death and that cases in which the loss of blood in itself would be sufficient to bring about a fatal termination would seldom be seen in time to save the patient. He bolsters his position by animal experiments, having observed that dogs do not die of hemorrhage even after section of the uterine and ovarian vessels.

Just what he considers the cause of death in these cases is not clear. The coroner's statistics of Dr. Formad, though he admits that it is on record that in certain instances the amount of blood which was found was enough to fill the abdominal cavity, Robb dismisses by saying that "such statements are entirely too meager to give us any definite knowledge, nor can they be entirely depended on." He also says in this regard that "in a given fatal case it must also be proven that there were no other and possibly equally important factors in the causation of the fatal result." He not only doubts that the coroner saw the blood, but he invites us to prove that the patient did not die of cerebral apoplexy instead of abdominal hemorrhage. As for the animal experiments I can only say that, if he has not seen a woman die from hemorrhage from a uterine artery, he has been more fortunate than I have been, and that I therefore still resort to the old-fashioned expedient of tying as secure a knot about that vessel as I am able. JOHN B. DEAVER.]

Formerly it was not such an uncommon thing for these patients to bleed to death. Of the 500 cases reported by Parry there were 336 deaths, 174 of which were from rupture and hemorrhage. Of 113 of these in which the time of death was stated 81 had died at the end of 24 hours and at the end of 48 hours only 15 were left alive.

Of course this gives a greatly exaggerated idea of the danger because in those days only the evident and severe cases were noted. Still it serves to show that, without operation, death, which was shown by autopsy to be associated with excessive hemorrhage, was not so uncommon a sequel. If these deaths were not due to hemorrhage, what did cause them?

[Has anyone seen a death from shock of rupture with an insignificant or even a moderate amount of blood in the peritoneal cavity? In the cases which I have seen in this so-called state of shock, the condition of the patient bore a striking parallelism with the amount of blood found in the abdominal cavity. I wish to enter a strong protest against the loose use of the term shock in this condition as well as the vicious tendency of such flashy phrases as "adding shock to shock. JOHN B. DEAVER.]

The great danger in these cases is not from the shock of rupture, but from the subsequent hemorrhage. Or, to be very conservative, severe hemorrhage is necessary to produce the fatal outcome. Let us consider for a moment this factor, shock. It is known that any acute lesion of the peritoneum produces, through shock to the great abdominal nerve centers, a certain train of symptoms, whether the lesion be due to rupture of the appendix, twisted pedicle of an ovarian tumor, passage of gall-stones, acute strangulation of the intestine, or rupture of an extra-uterine pregnancy, and to this train of symptoms Gübler has given the name "peritonism." These symptoms are independent of inflammation or of septic intoxication. They are: pain, profound exhaustion, distressful anxiety, pallor; soft, quick pulse; cold extremities, shallow respiration, nausea and vomiting. These vary in degree and are common in some degree to all cases in which there has been a wide

and abrupt impression upon the nerve centers of the abdomen. This is the train of symptoms which follow immediately upon an acute rupture of the gestation sac and gives the picture properly denominated as shock. This shock as such is practically never fatal. Clinical evidence is conclusive on this point. We do not find our patients dropping over dead from acute strangulation, twisted pedicles or tubal ruptures. The shock exerts its maximum influence at the moment of the tearing injury to the peritoneum and sympathetic trunks and practically ceases at once with the release of tension after the laceration has been effected. This factor is sudden, momentary, expends its energy and ceases. Reaction begins, or would begin at once, either spontaneously or with the aid of stimulants. This sudden insult to the peritoneum and the great sympathetic centers is not what places the patient's life in jeopardy and holds her hovering in the balance for hours.

This is but the advance agent of the real executioner, hemorrhage. Read in the same order as before, leaving off the pain in the beginning, we have in the symptoms of shock the symptomatology of hemorrhage: Profound exhaustion, distressful anxiety, pallor; soft, quick pulse; cold extremities, shallow respiration, air hunger, nausea and vomiting.

[Who is that man who will tell us in these cases where shock leaves off and hemorrhage begins to play the leading rôle? I feel most strongly that we are dealing here with a wrong use of words, that there is a sophistical "nigger in the woodpile." I do not believe that the patients reported by the advocates of the expectant treatment as suffering from shock were suffering from primary shock, but instead from shock plus hemorrhage, and that, by the time they were seen by the surgeon, that hemorrhage was playing by far the chief rôle. Those patients who are fortunate enough to lose but a small quantity of blood at the time of rupture react from the shock with considerable promptitude. By the time proper surgical intervention can be brought to bear, their condition is such as to give the surgeon little immediate anxiety as far as the shock of operation is concerned. These patients should be operated at once on account of the danger of secondary rupture or a renewal of bleeding. They should all get well. John B. Deaver.]

An immediate operation detracts nothing from the chances, but guards against imminent danger. Those patients who, when seen an hour or several hours after rupture (I am speaking of conditions as we find them, for patients do not come to a hospital or doctor's office to be handy at the time of rupture), are hanging in the balance with the symptoms some are pleased to call shock are not suffering from shock, but rather of shock plus hemorrhage, shock in small type, hemorrhage in large red capitals, and the examples of reaction are not proofs of the wisdom of waiting, but of the fact that many desperate cases will stop just short of bleeding to death if left to themselves, a fact which has for years been patent to all.

After operation for tubal pregnancy patients became again pregnant in 35.19 per cent. of the cases, but only 18.5 per cent. of these are extrauterine. Out of 4526 cases of tubal pregnancy a recurrence was reported in 4.68 per cent. H. A. Dietrich (Zentralbl. f. Gynäk., Apr. 9, 1921).

There are certain factors which would favor the cessation of bleeding, such as a long and voluminous sigmoid or omentum wedging down in the pelvis, but, as we are not often

furnished with a diagram of interior arrangements in these cases, we do not know whether these stanch allies are on the ground. The character of the rent and the coagulability of the blood we cannot estimate.

[As sure as there are immutable laws of hydrostatics and of the circulation of the blood, these patients have died in the past in considerable numbers from hemorrhage and occasionally die today from that cause, and the only reason more do not die of it is because of the early operation practised by clinical surgeons.

I am willing to grant that a patient should not have a "penknife" operation done on her before she has recovered from her first faint. There is reason in all things. It is equally true that a patient in *articulo mortis* should not be subjected to operation. "The resources of surgery are rarely successful when practised on the dying. These principles, however, should not be made use of to attack a mode of treatment which has been crowned with the highest success." John B. Deaver.]

The treatment of unruptured ectopic is operative as soon as the diagnosis has been made. After rupture has taken place, operation should be postponed until the patient has recovered from the shock incident to the hemorrhage following rupture. Almost all of these patients will "come back" with rest and morphine. They are given an initial dose of ½ grain (0.03 Gm.) of morphine, followed by ¼ grain (0.016 Gm.) every 3 hours until the respirations are reduced to from eight to twelve per minute. The writer has yet to see a case which has not reacted and become a safe operable risk under this treatment.

The operation is always done by the abdominal route and the tube either emptied of its contents or amputated. In the removal of the tube great care should be exercised in individually ligating the vessels in the mesosalpinx so that the collateral circulation to the ovary is not interfered with. "After the tube is removed, the ovary is suspended by suture of the infundibulopelvic ligament to the round ligament and the raw surface at the top of the broad ligament peritonealized by whipping the mesosalpinx and round ligament together. J. O. Polak (L. I. Med. Jour., xii, 121, 1918).

My position then is this: A continuance of the collapsed condition, commonly, and as I believe erroneously, termed shock, for a longer time than one hour indicates that a considerable hemorrhage has occurred and may be continuing. The surgical indications are clear—stop the bleeding; stimulate. Let us not revert to the dark ages in the ranks of those who "watched the life ebb rapidly from the pale victim of this accident, but never raised a hand to help her."

According to Schauta, the maternal mortality in non-operative cases is 68.8 per cent. The writer is inclined to feel that this percentage is too high, that more cases of ectopic gestation escape recognition and live than we have suspected. At the Columbus Hospital operation is always resorted to, and, performed speedily and promptly, should not give a mortality of over 2 per cent. The dangers are from shock, hemorrhage, sepsis, exhaustion, and intestinal obstruction. J. M. Keyes (N. Y. Med. Jour., Aug. 6, 1910).

Since 1900 I have had 110 cases of extra-uterine pregnancy, many of them of the acute type, without a death.

My procedure in these urgent cases is as follows: If the condition be very low, stimulation is begun on admission by hypodermoclysis and strychnine. If there is extreme restlessness, morphine is a valuable adjunct administered, of course, with due discretion.

Tubal Pregnancy. (*J. B. Deaver.*)

They are placed on the table with as little disturbance as possible and a light quick etherization given. Preparation is rapidly completed and intravenous transfusion of **normal saline solution** started as the abdominal incision is made. "Get in quickly, get out quicker" applies here as forcibly as anywhere in surgery. The offending tube and ovary are removed. The clots are scooped out, and, if the condition of the patient warrants, the abdomen is flushed out and filled with normal saline before closure.

> The writer divides ectopic gestations into 4 groups, viz., with negligible, moderate, severe, and fatal hemorrhage. Patients of the first group frequently recover spontaneously. If the hemorrhage is discovered, the **operation** can be deferred until the peritoneal irritation subsides. In the third group, shock is great. The pain should be relieved by **morphine,** the head lowered, and the extremities bandaged. A donor should be procured for a blood **transfusion,** which is to be started before the incision is made in the abdomen. The fourth group of cases bear transportation poorly. Infusing these patients with **saline solution** to which 6 per cent. **gum acacia** has been added will restore the circulation until the patient can be taken to the hospital. Hermann Grad (Trans. N. Y. Acad. of Med.; Med. Rec., Dec. 4, 1920).

I have frequently seen the patient go off the table with a far stronger pulse and in better condition than before the operation, a sufficient refutation of the charge of "adding shock to shock." I have rather refused to allow hemorrhage to be added to hemorrhage, and now I am not afraid to fill her vessels with sufficient fluid to satisfy the mechanical needs of the circulation.

[My last case before this article was written happened to be most appropriate to this discussion: A young woman, aged 24, married three years, with nothing of note in her past history. She had had one child nine months ago, which died in January. No miscarriages. Menstruation had always been regular and normal up to her January period, which she missed. At the February period she bled quite profusely and for a longer time than usual. No staining since. Suddenly at 6 a.m. on February 12th, during coitus, she had an acute pain in the lower left side of the abdomen, followed in a few minutes by syncope. Soon she recovered, but fainted several times in the course of the morning, and vomited several times. Gradually grew weaker and grew short of breath. On examination she did not have a particle of color in her skin or lips. Expression was anxious: she was restless and dyspneic. The pulse was about 180 and barely perceptible. Her abdomen was moderately distended and tender in left side low down. Vaginal examination was negative except for tenderness in the left lateral fornix.

She was taken to the operating room and subcutaneous infusion started with the ether. Preparation having been quickly accomplished, the operation and intravenous transfusion were started together. A left-sided tubal pregnancy (see colored plate) the size of a hickory nut was found in the isthmial portion about 2 cm. from the cornual extremity. Through the tube was a perforation only about as large as a pinhead. No time was wasted in determining whether there was any active bleeding. Tube and ovary were removed. As the patient's condition was improving on the table, I washed out the blood, of which there was a large quantity, and filled the abdomen before closure with salt solution.

Her pulse, which before the operation was 180, at the end of the operation was 140 and much improved in quality. She was put back in bed and continuous proctoclysis started. JOHN B. DEAVER.]

I wish to call attention to the value or rather necessity of filling the empty blood-vessels with saline in these depleted cases. In the above case, the amounts used were as follows: By hypodermoclysis at the

beginning, 1000 c.c. Intravenous transfusion during the operation 2000 c.c. Left in the abdomen at least 1500 c.c. Then in the twelve hours after operation her thirsty vessels absorbed by way of the large bowel 4000 c.c. additional. Nearly nine liters of saline, over two gallons of fluid to meet the mechanical needs of the circulation. Without this saline my patient would have run grave danger of dying on the table. As the intra-abdominal pressure is released by incision the blood flows into the "splanchnic tank" and from the great depletion due to hemorrhage nothing is left in the great vessels for the heart to pump. The medullary vessels are asphyxiated and death results. This restoration of the fluid volume of the blood is a most important point.

In 12 out of 135 operative cases of extra-uterine pregnancy, the writer reinfused into a vein 300 to 1000 c.c. of the woman's own blood, diluted with an equal amount of physiologic salt solution with a little sodium citrate. The blood was scooped or soaked up from the abdominal cavity, passed through a funnel over some gauze as a filter, and then into a receptacle containing salt solution. One woman died of peritonitis—the only death in 12 cases. Von Arnim (Zentralbl. f. Gynäk., Nov. 29, 1919).

The writer has likewise had good results from reinfusion of blood in tubal abortion or rupture of the spleen. He punctures the abdominal wall in the lower third of the rectus muscle and aspirates, to confirm the presence of fluid blood. The infusion tube is introduced into the vein by the assistant as the abdomen is being opened. The parietal peritoneum is then drawn up into a cone and the blood around the bladder runs out. From one-half to 1 liter of fluid blood is thus secured in a few minutes,

strained, citrated and poured into the infusion funnel. Kulenkampff (Zentralbl. f. Gynäk., Apr. 17, 1920).

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ABSCESS.—DEFINITION.—A circumscribed collection of pus in an adventitious cavity, the result of localized inflammation due to infection by pus-forming microbes, differing from *diffuse suppuration* which is not circumscribed and from *purulent effusion* or *empyema* which is found in a natural or pre-existing cavity, as the pleura, pericardium, mastoid cells, etc.

VARIETIES.—An abscess may be *acute,* or *warm,* when due to pus-microbes only: staphylococci, streptococci, and others; *chronic,* or *cold,* when due to a specific microbe, especially that of tuberculosis.

Abscesses have been classified according to :—

1. Etiology. — Atheromatous, embolic, fecal (stercoraceous), metastatic, miliary, ossifluent, puerperal, pyemic, residual, symptomatic or congestive, tropical, tubercular (strumous, lymphatic, or scrofulous), etc.

2. Pathology. — Acute or warm, canalicular, caseous, chronic or cold, critical, gangrenous (anthrax), ligneous, perforating, phlegmonous, etc.

3. Location (Organ or Tissue Involved).—Alveolar (gum, jaw, teeth), of axilla, bone (subperiosteal), brain (cerebral, cerebellar), bursal, corneal (hypopyon), deep, dorsal, follicular, hepatic, of hip-joint, iliac, ischiorectal, lacunar, lumbar, mammary (milk, weid or weed, breast), marginal, mediastinal, meningeal (extradural, subdural), of neck, nephritic and perinephritic, of nose, of palate, palmar, of pancreas, perityphlitic, popliteal, of prostate, psoas, rectal, retropharyngeal, of skin

(furunculosis), of scalp, of space of Retzius (properitoneal cavity), spinal or vertebral, of spleen, superficial, thecal, urethral and periurethral, vulvo-vaginal (Bartholinian), etc. All the above varieties will be considered under their respective anatomical heads.

ACUTE, OR WARM.—Symptoms.—An acute abscess may be either superficial or deep. When it is superficial the local symptoms predominate; when it is deep the general symptoms are more marked.

The pain, due to compression of the nerves by the disturbed tissues, varies in degree with the density of the parts involved, the local supply of sensitive nerves, and the tension produced by the inflammatory products. In superficial abscess the pain is generally localized in the center of the swelling, and is sharp and lancinating; in deep abscess it is more diffuse and dull.

Redness is due to engorgement of the local blood-supply, and the swelling to the inordinate distention of the vessels and the secondary escape of blood-plasma, colorless corpuscles, etc., into surrounding tissues. It may become very great in certain regions, such as the lids, the lips, etc., in which the cellular tissue is lax. As the purulent foci run together and form a single cavity, the center of the tumefaction becomes soft, and darker in color, and the abscess is said to be "pointing."

Edematous infiltration in superficial abscess denotes the presence of pus; in deep abscess subcellular edematous infiltration is an important sign of deep suppuration.

Local heat, throbbing, and tension are mechanical results of the causes of tumefaction tending to decrease as the formation of pus progresses.

Hyperpyrexia is in relation with the location of the abscess, the ease with which the pus-microbes can enter the circulation, and the amount of pus and necrotic tissues present. In superficial abscess there is but little rise of temperature, but in deep abscesses it sometimes reaches 104° F. (40° C.) at the time the wall of granulation tissue is established. A remission of about one degree each morning usually takes place. When the pus has found an issue, or has become completely surrounded by the limiting membrane, the intensity of the fever is usually reduced.

In a superficial abscess, if a chill occur, it is usually very slight, and appears between the fourth and the eighth day. It indicates the formation of pus. In a deep abscess a chill generally occurs, lasting from a few moments to half an hour.

Fluctuation is generally obtained when the purulent focus has been formed. A sharp localized pain on pressure over the apex of the swelling obtained at this time supports the likelihood that pus is present, but fluctuation is liable to be a misleading symptom.

Interference with motion or the normal functions of a part is sometimes produced through the proximity of an abscess.

In deep-seated abscess any or all of the general symptoms of abscess may be lacking, except loss of flesh and strength. This is especially true of hepatic or cerebral abscess. The symptoms usually present are local tenderness and pain, pressure symptoms, overlying edema, brawniness, muscular rigidity and ankylosis of neighboring joints, in addition to the symptoms of acute suppuration—fever, chills, sweats, anorexia, restlessness, etc.

Etiology.—Inflammation due to traumatisms and lesions of all kinds, especially the introduction of foreign bodies under the epidermis, are the usual causes of abscess. While blows do not apparently produce superficial lesions in the majority of cases, the fact remains that an invisible abrasion may be present and serve as a channel for the introduction of the pyogenic organism. The cutaneous glands, through weakened local resistance, may also become the transmitting media. Any cause removing the epithelial layer of the mucous membrane may also form the primary etiological factor of an abscess in the membrane or in the submucous connective tissue. Abscesses also arise in connection with the various septic fevers.

> The writer refers to 2 cases of inflammatory newgrowths of extremely slow development which had led to the diagnosis of cancer. They were hard and located in the abdomen in both instances. The patients were men of 26 and 72. The tumors were observed 4 years and 3 months, respectively, and both were permanently cured by clearing out the focus. There was a history of operative treatment for inguinal hernia not long before in each case, but in the younger man unsuspected appendicitis was probably the main factor. In both cases only the ordinary pyogenic germs were found. Filardi (Policlinico, Aug., Surg. Sect., 1917).

The three essentials in the formation of an abscess are: pyogenic organisms in sufficient numbers and virulence, their proper implantation within the tissues, and a sufficiently low resisting power, either local or general.

Pathology.—While several varieties of micro-organisms are found in the pus of an acute abscess, the principal ones which ordinarily cause purulent inflammation are the *Staphylococcus pyogenes* (*aureus* and *albus*), *Streptococcus pyogenes, Micrococcus gonorrhœæ, Bacterium coli commune, Bacterium pyocyaneum, pneumococcus,* and the *Sarcina tetragena.* Less frequent in the production of suppuration are the typhoid bacillus, the influenza bacillus, the diphtheria bacillus, the actinomyces, etc.

> An acid-fast bacillus was cultivated by the writer from chronic intractable pustules covering the back, buttocks, and thigh of a soldier returned from France. No micro-organisms were seen in the pus, and none could, at first, be cultivated from it. But subsequently there was grown, on more than one occasion, the acid-fast bacillus referred to. Cobbett (Brit. Med. Jour., Aug. 17, 1918).

According to Kreibich suppuration can occur in man without the presence of bacteria. Both in animals and in man, suppuration may be due to the irritation of chemicals. Investigators have shown that suppuration is only a certain stage of inflammation, not a separate qualitative form of inflammation. The serous formation of blebs and bullæ becomes purulent without the presence of bacteria.

Chronic suppurative processes are, according to Lyman·Allen, very frequently unattended by fever, while acute suppurative processes are frequently unattended by fever. In a given case, therefore, the absence of fever must have little weight by itself in excluding the possibility of suppuration. Since a rise of temperature above 100° F. occurs in about two-thirds of all aseptic cases, the presence of fever *alone* must have little weight in making a diagnosis of suppuration.

Suppuration is almost invariably preceded by inflammation due to the

pyogenic micro-organisms. The first effect of the bacterial toxins on the local circulation is to cause an increased rapidity of the flow of blood in the part, the vessels becoming engorged and dilated. This is succeeded by slowing of the current and passage through the vascular walls and into the surrounding tissues of colorless corpuscles (leucocytes), a few red corpuscles, and blood-plasma, the latter of which become coagulated and finally softened. One or several cavities are thus formed; but, if the cavities are multiple, the barriers usually soften and a single focus is established. The pus is composed of the corpuscles which perish in the cavity thus formed, the broken-down remains of tissue, and the plasma. At a distance from the location of the abscess the circulation is normal, but, as the diseased area is approached, the slowing of the blood-current becomes gradually more evident, until a zone of living leucocytes is met, forming a protective barrier around the abscess cavity. The surrounding parts also become permeated with new vessels, and a zone of granulation tissue (the pyogenic membrane of older writers) is formed. The spread of the suppuration being thus checked, the pus is forced to the surface because it finds the least resistance in that direction; but, if an aponeurosis or fascia interfere, it burrows until an exit is found.

The rôle of the white corpuscles (leucocytes) has been interpreted in various ways; Cohnheim considered them as elements of repair; others have attributed to them the rôle of scavengers. The accepted theory at present, however, is that of Metchnikoff, who considers them able to attack and destroy invading organisms. The process is termed by him *phagocytosis,* the cells

being called phagocytes (φαγω, to eat, and κυτος, a cell).

The dead leucocytes in pus must be looked upon as the cells that have been brought up rapidly to interfere with the spread or diffusion of the products of the micro-organisms; a large number of these cells coming in contact with the poison in a concentrated form may succumb to its action; but before doing so they are able to deal with a certain quantity of the poisonous material, breaking it down and rendering it inert. Other cells are constantly being brought up to assist these, until, at length, the bacteria are completely hemmed in. They live for a short time on the dead tissues; but, being localized by the barrier of leucocytes, they ultimately die, either from inanition or because they are poisoned by their own products or by immunizing constituents of the blood-plasma. It is found very frequently on opening an abscess that no organisms can be seen, those that were originally present appearing to have undergone degenerative changes and to have been taken up by the phagocytes, or devouring cells.

The process includes, according to Sajous, participation of the proteolytic or peptonizing action of enzymes in the serum supplied in large quantities to the abscess. The prevailing view is that these are produced by the pyogenic bacteria. From his viewpoint (see "Internal Secretions," vol. ii, 4th ed., 1911, p. 907) these ferments are secreted (though originally derived from the pancreas, thyroid, and adrenals) by phagocytes (Metchnikoff's trypsic cytase), themselves and their liquefying action has for its purpose to destroy the bacteria and their toxins in the abscess. The pathogenic organisms are first sensitized and softened by opso-

nins and agglutinins (thyroid secretion), and thus rendered vulnerable not only to the digestive action of the phagocytes when ingested by these cells, but to the ferments (trypsin mainly) they contribute to the abscess fluids, in which they accumulate in large numbers.

Differential Diagnosis. — Fluctuation only indicating the presence of fluid, the presence of this sign without the other symptoms mentioned should inspire great circumspection, especially if surgical measures are employed.

ANEURISM is the most dangerous condition to fear. It has, however, a less acute history, a peculiar thrill and expansile pulsation, and can only exist in close proximity to a large vessel.

Certain SEMISOLID GROWTHS may simulate an abscess. When the possibility of an aneurism has been eliminated, a fine trocar or exploring needle, if carefully used, will determine the diagnosis.

Prognosis.—This depends upon the general health of the patient. In the robust a suppurative process usually reaches the stage of resolution without giving rise to complications. In individuals weakened by disease, hereditary or acquired, an abscess may be protracted and exhaustive, and diffusion is more likely to occur if resisting tissues interfere with the superficial evacuation of the pus. Deep abscesses are especially prone to become protracted through this cause, the resistance of muscular aponeuroses, etc., forcing the pus into the cellular interstices. Fistulous tracts, or large suppurative areas, are thus created, and the patient may succumb to blood poisoning or its consequences.

Treatment. — *General Measures.*— Rest and elevation of the affected region, if possible; salines, if purgation is necessary. Easily assimilable food, but not low diet; avoidance of stimulating beverages, alcohol, coffee, etc.

Internal Remedies.—If the case is seen early the suppuration can sometimes be arrested by the use of one of the following agents, supplemented by one of the local applications: Tincture of **aconite,** 3 to 10 drops every hour, closely watching the patient's pulse; tincture of **veratrum viride,** 1 drop every hour until the pulse becomes slower, the skin moist, and slight nausea occurs; or **calcium sulphide** (sulphurated lime), $\frac{1}{10}$ grain every hour; or, again,

R *Sulphate of quinine,* 1 grain.
　Ext. of nux vomica, $\frac{1}{4}$ grain.

For one pill, to be taken every three hours.

Many incipient abscesses disappear under the internal use of the **hypophosphites** of potassium, sodium, and calcium. They also act as an excellent prophylactic, if given before pus has formed. Tousey believes them to be more efficient than **calcium sulphide.** The combination used by Tousey is 5 grains of calcium hypophosphite, and 2 grains each of the sodium and potassium hypophosphites, administered in syrup or two capsules, followed by half a glassful of cold water.

Fresh **brewers' yeast** in doses of ℨj to ℨij in water or undiluted, just before or during meals, is a favorite remedy with many, although diarrhea sometimes results, even when the yeast is fresh. A substitute preparation is made by macerating compressed yeast in water. Desiccated yeast is also used.

In addition to these internal remedies, we should not forget that stimulation, nutrition and general hygienic measures are of considerable value.

Thyroid gland in doses of 1 or 2 grains three times daily hastens the disappearance of abscesses, by increas-

ing the proportion of opsonins in the blood (Sajous).

Ferges and Gergo recommend the use of fresh **normal blood-serum** from the horse or from cattle in the local treatment of acute suppurative processes in 100 cases. The pus was first aspirated, serum next injected to rinse out the cavity, using a needle closed at the end, but with a row of openings just above it; then the excess of fluid aspirated, and the opening covered with a bit of sterile gauze held by adhesive. It is important that all the excess of serum be removed from the cavity; otherwise, symptoms of serum intoxication may follow. The serum apparently produces both a passive and an active immunity, stimulating leucocytosis and phagocytosis. Better healing can be obtained by this method, according to the authors, than in any other way. Acute abscesses in the soft parts, whatever be the micro-organism present, show especially good results. One treatment with the serum generally suffices.

External Remedies.—The surface is carefully cleansed with **antiseptic soap** and sprayed with a 2 per cent. **carbolic acid solution,** or with **hydrogen peroxide,** every two hours, the atomizer being used for ten minutes at each sitting. (Verneuil.)

Compresses dipped in hot 1 : 4000 **corrosive sublimate solution** are very effective. If abscess is upon an extremity, a 1 : 4000 **corrosive sublimate solution** may be employed as a bath for the limb, the latter being left in the solution several hours at a time.

A solution of **nitrate of silver** (30 grains to the ounce) may be applied frequently with a camel's hair pencil.

Tincture of **iodine** may be applied in the same manner every three hours.

When the surface becomes very tender, **belladonna ointment** may be rubbed in every two hours.

In abscesses characterized by very severe pain a 10 per cent. solution of **cocaine** may be introduced **by cataphoresis,** the anode sponge of a galvanic battery being applied to the part. The sittings should last five minutes, and be repeated every three hours, the current not exceeding 5 milliampères. During the intervals **warm fomentations**—with borated, camphorated, or pure water—are of great value.

Encouraging results obtained in the treatment of tendon-sheath phlegmons and suppurating inflammation in general with **superheated air,** applied with an ordinary apparatus. It is used twice a day for two or three hours each time, maintaining a temperature of from 90° to 110° C. (194° to 230° F.) within the frame at half its height. Thus arranged, the temperature on the skin averaged 44° or 47° C. (111° or 116° F.), and the acceleration and sweating induced seemed to keep the temperature of the skin within due bounds. The applications of the hot air are made the day after the abscess has been incised and evacuated, and the cavity packed with iodoform gauze. He also states that neglected injuries of the fingers which would otherwise have necessitated amputation healed under this hot-air treatment without requiring operative measures, and recovery was hastened. This treatment also caused an abolition of pain. (Zentralblatt für Chir., Oct. 24, 1908.)

Pads of gauze wrung out of **hot boric acid solution** (an ounce to a quart of water), applied as hot as the patient can bear them, and well covered with oiled silk to keep in the heat and moisture, are the best; wherever applicable, as with the hands or feet, the inflamed part should preferably be submerged every hour for a period of five to ten minutes in the hot boric solution itself.

The application of a **sheet of zinc**, the thinnest possible, cut to fit the shape of the lesion and applied directly to it, was found exceptionally effectual by the writer, who attributes the results to the ions generated by the different nascent compounds of zinc. The metal is held in place with a dressing which is left undisturbed for 5 or 7 days. Any tendency to hypertrophy of the edges of the lesion calls for cauterization. Long rebellious cold abscesses yielded promptly to this measure. C. H. Sztark (Arch. de Méd. des Enfants, Oct., 1918).

Wright's Bacterial Vaccines.—Treatment of staphylococcus and streptococcus infections (abscess, suppuration, etc.) by the therapeutic inoculation of staphylococcus and streptococcus vaccines, as suggested and developed by Sir A. E. Wright, of London, has found many endorsers. A bacterial vaccine is a sterilized, standardized emulsion of the infecting micro-organism. It is made by scraping the film of a recent agar culture into a 1 per cent. salt solution, sterilizing at 60° C. (140° F.), and subsequently standardizing to a given number of micro-organisms per cubic centimeter. The method is, however, a new and complex one, and, until its use has been more thoroughly explored, it should only be employed under the guidance of an expert. Whether an opsonic control of the injections will always be necessary still remains to be shown, but in all cases the use of the vaccines should be preceded by a most careful bacteriological examination, and the particular vaccine should be prepared for each individual patient. The dose of staphylococcus vaccine is 100 to 1000 millions; an inoculation being made every ten days. The dose of streptococcus vaccine which is more toxic than staphylococ-

cus is 20 to 60 millions; the inoculations being repeated weekly or every two or three weeks.

Case of furunculosis, subperiosteal abscess of the head, and necrosis of the bones of the skull treated by operation and **autogenous vaccine.** *Staphylococcus aureus* was recovered from the parietal abscess and from the blood. An autogenous vaccine was made, and 4 doses were given at intervals of four days. The first dose was 50,000,000, the second 100,000,000, and the last 2 150,000,000. With no constitutional reaction, the local condition rapidly improved. The general condition of the patient improved, but a portion of the bone at the base of the abscess was denuded and necrosed. At a later date this sequestrum was removed and the patient was given 3 more injections of the autogenous vaccine at four days' interval, each dose being 150,000,000. Within three weeks the patient was in normal condition. The author urges preference for the autogenous vaccine. G. G. Ross (Monthly Cyclo. and Med. Bull., Sept., 1910).

Bier's hyperemic treatment (passive congestion or artificial hyperemia) of acute abscesses has given excellent results as to immediate relief of pain and reduction of inflammation.

Inflammation, according to Bier, does not in itself represent a diseased condition, but is a phenomenon indicating the body's attempt to resist a deleterious invasion. To increase this beneficent inflammatory hyperemia resulting from the fight of the living body against invasion, is the aim of Bier's hyperemic treatment. The blood must, however, continue to circulate; there must never be a stasis of the blood. Bier's method artificially increases the redness, heat, and swelling, three of the four symptoms of acute inflammation. He discards all means that tend to subdue inflammation.

Bier produces this hyperemia by any

or all of three methods: Elastic bandage or band, cupping glasses, and hot air. In the use of the elastic bandage, it should cause slight obstruction to the return of the blood, but not sufficiently firm as to obliterate the pulse beat below or be in the least way annoyable to the patient.

The technique is correct if there is absolutely no increase of pain, and if there is visible hyperemia of the parts subjected to treatment; the portion distal to the bandage must appear bluish or bluish red—never white. All dressings should be removed while the compressing elastic bandage is in place, the wounds or bruises being covered with sterile gauze kept in place by a loosely applied towel. Under hyperemic treatment any abscess must be opened and pus evacuated.

Acute inflammatory processes require application of the hyperemic treatment for twenty to twenty-four hours per day. In chronic cases, especially if tuberculous, shorter sittings, from two to four hours per day.

In the use of suction apparatus or cupping glasses to produce obstructive hyperemia, the skin should turn red or bluish red, but never white; circulation must not be interrupted. The vacuum apparatus of large size is supplied with a suction pump. These suction glasses are applied for five minutes, six times daily, with intervals of three minutes between applications, in order to give the edema and hyperemic swelling an opportunity to disappear. Thus the entire time of treatment is three-quarters of an hour each day.

Treatment of acute abscess by **passive congestion** has given excellent results. Cases of purulent arthritis, suppuration of tendon sheaths, and acute abscesses and carbuncles have shown without exception almost immediate relief of pain and reduction of inflammation. The abscess either became "cold" or its contents changed to serum or were resorbed. Purulent arthritis was treated with passive motion after all pain had been relieved. The writer selected 15 of the 110 cases cited for brief description in the article. All cases were quickly cured, and it was only rarely necessary to open the abscess. Of the 15 cases reported, 8 were resolved, 3 were opened, and 4 were discharging when admitted. Bier (Münch. med. Woch., Jan. 31, 1905).

By means of **artificial hyperemia** we can often abort an infective process and save the breaking down of tissue, or, if at the beginning of treatment the process has gone on to the breaking down of tissues, the hyperemic method assists in quickening the process of expulsion of the products of infection and also the process of repair. J. H. Beaty (Jour. Minn. State Med. Assoc., Jan. 15, 1908).

In the use of hot air to produce hyperemia we produce an arterial hyperemia which differs from the obstruction or venous hyperemia. The effect of **hot-air hyperemia** is also different upon the body and also upon the pathologic process. This last method is apparently not used in the treatment of abscess.

The author comments on the value of **Wright's solution of sodium chloride**, 4 per cent., **and sodium citrate**, 1 per cent., as an agent for promoting drainage of abscesses. The hypertonic solution of sodium chloride by osmosis brings about a flow of lymph through the abscess walls, while the sodium citrate, by precipitating the calcium salts in the lymph, prevents the latter from clotting, and thus perpetuates the discharge. The lymph and 4 per cent. salt solution both antagonize the bacteria.

The technique of treating an abscess by this plan is described as follows: The abscess is opened by a wound as small as will allow the cavity to be wiped out, or thoroughly emptied by

expression. The surrounding skin is well cleaned with 70 per cent. alcohol and smeared up to the very mouth of the wound with boric acid or eucalyptus vaselin, in order to avoid skin irritation from the salt solution. If the skin tension closes the opening a bit of rubber dam may be put in. The wound is covered with a voluminous pad of gauze or of absorbent cotton covered with gauze, dripping wet with hot salt and citrate solution. A many-tailed bandage or some other application holds the poultice in position, and the part is put at rest. Outside the dressing may be applied a hot flaxseed poultice or a hot-water bottle. In any case, as often as the dressing gets cold, more of the hot solution is poured over the whole dressing to wet and warm it again, or the dressing is removed and the whole part soaked, if possible, or bathed with the same solution.

The solution is contraindicated if there is a tendency to persistent oozing of blood from the wound, and where the formation of protective adhesions is desirable.

Inguinal and axillary bubo, abscess of neck, septic fingers, mastoid wounds, otitis media after paracentesis, all drain well under this method. The solution should be used only for the first thirty-six to seventy-two hours after operation, during the acute stage of inflammation. The wound is then filled with glycerin or balsam of Peru. Crandon (Annals of Surg., Oct., 1910).

The **iodoform bone-wax** recommended by von Mosetig-Moorhof tried in 5 cases, in which the wax failed and was discharged. It is of value as a filling in selected cases of circumscribed abscess cavities in bone. Its use shortens the convalescence and makes the dressings easy and painless. Simmons (Annals of Surg., Jan., 1911).

Bismuth paste injection is an agreeable procedure, practically painless and free from risk, and of value in the treatment of chronic fistulæ and abscess cavities. H. H. Schmid (Wiener klin. Woch., Nu. 7, 1911).

The writer tried the effect of **X-rays** upon a case of chronic suppuration of very long duration, which had resisted other forms of treatment, including surgical operation. The suppuration was arrested, the part was healed, and the cure has lasted to the present time. Several other cases of a similar kind were then treated, and recovery obtained. Cumberbatch (Lancet, May 16, 1914).

In pyogenic infections the defensive tissue reaction awakened is purely local, general reactions being but slightly marked or absent. In order to be able to inject the germs in an absorbable form, the writer combines the Pasteur method of ageing cultures with the modern procedure of sterilization of cultures by heat. Much larger doses of the **Delbet vaccines**—billions—of germs can thus be injected, without producing any "negative phase." On the other hand, severe reactions similar to Widal's "hemoclasic attacks" often result; though manifestations of toxicity, these reactions are often a favorable indication. In one case an injection of 20 billions of germs in a case of very grave phlegmon of the hand was followed even by dyspnea, asphyxial attacks, and cyanosis; but within 24 hours the local condition improved and recovery very rapidly followed. Experience has shown that the best dose of the vaccine is 4 c.c., containing about 13 billions of bacteria. The vaccine used is a stock preparation containing streptococci, staphylococci and pyocyaneus germs —the latter in large number, 8 billions. The author does not believe in an essential specificity of vaccines; Wright has, himself, given up autogenous vaccines, and has even expressed a suspicion that vaccine prepared with a germ different from that causing an infection gives better clinical results. The pyocyaneus germ is chosen because it plays a useful rôle in relation to the streptococcus, hindering its development and attenuating its effects. In the last 6 years no case of *carbuncle* has been incised

in the writer's service. Recovery from *boils, lymphangitis,* and *erysipelas* is rapid under the vaccine treatment. *Lymphangitic abscesses* are given combined incision and vaccine treatment. Once sterilization has been secured, the wound margins are brought together with plaster strips to accelerate healing. *Adenitis* disappears in a few days under the treatment, or else softens very rapidly, so that after evacuation through an incision the parietes promptly come together again. This method is frequently indicated in abscesses of the wisdom teeth, in which the relative degree of the glandular and the periosteal involvements is difficult to define. In subacute *osteomyelitis,* the procedure gave successful results in 3 out of 6 cases. Good results were likewise obtained in *acute salpingitis.* Recently definite improvement was noted in cases of *gonococcic arthritis,* although specific serum had failed. Delbet (Presse méd., Feb. 7, 1920).

Antiferment Treatment.—This so-called "physiologic treatment" of abscess was introduced by. Müller and Peiser. It is based on the antagonistic action the proteolytic ferment derived from leucocytes is supposed to meet from an antiferment in the blood-serum, especially in morbid effusions. This antiferment can be obtained from the patient's own blood-serum, after venesection or from puncture fluids. The contents of the abscess being aspirated, the antiferment is then injected into the cavity with the same needle, enough being introduced to fill it without distending it. The contents of the abscess are then again removed and the cavity is once more filled with fresh antiferment. This is repeated the next day. if the area is still sensitive, the antiferment being left in.

The writer has tried the injection of **leucofermantin** into abscesses—a treatment based upon the fact that a proteolytic ferment is found in the polymorphonuclear leucocytes. A fairly large needle was used for aspiration and injection, and, after evacuating the abscess, he injected and withdrew a small quantity of serum, so as to clean out the cavity as thoroughly as possible before making the final injection, which was allowed to remain; a moist aseptic dressing was then applied. If the aspiration had to be repeated, the needle was inserted through the old puncture, so as to save pain. The quantity of serum left in varied, according to the size of the abscess, from 2 to 15 c.c. The author feels convinced that the principle on which the method is based is sound, and that it opens up a new pathway in the physiological treatment of suppurative inflammation. MacEwan (British Medical Journal, Jan. 22, 1910).

Antiferment serum exerts a slight degree of curative action upon suppuration, but must be brought into intimate contact with the whole of the suppurating surface. It is suited only for superficial, well-defined abscesses. Boit (Med. Klinik, Apr. 16, 1911).

Surgical Measures.—Incision and drainage tersely indicate the surgical treatment of acute abscess. If suppuration cannot be avoided, the abscess should be opened under rigid asepsis, as soon as an adequate quantity of pus has formed to constitute an abscess sufficient in size to be recognized by the surgeon as such (Senn), or as soon as the presence of pus has been determined by the exploring needle or syringe. An early incision prevents excessive loss of tissue, less deformity and leaves smaller scar.

If a local anesthetic is necessary, one of the following may be used: Twenty drops of a 1 to 5 per cent. solution of cocaine introduced sub-

cutaneously near the abscess; ether sprayed over the seat of the abscess until local numbness is experienced; chloride of methyl or chloride of ethyl vapor. The latter is especially efficacious; the parts turn white when ready,—generally in about two minutes. Seltzer water spurted over the surface may be used to advantage when none of the other agents can be obtained.

To open an ordinary abscess a single small incision suffices; but, if it is large, several small incisions should be made to render perfect evacuation of its contents possible by drainage. If the abscess is superficial, the skin alone should be cut, but if it is deep seated the skin and fascia should be incised and the grooved director, or the points of a pair of forceps, used to reach the pus, the opening being kept patent with forceps. The cavity is then thoroughly emptied and syringed out with 1 : 10,000 **corrosive sublimate solution,** or, better, with **normal salt solution** or **boric acid solution,** until the fluid comes out perfectly clear. Pressure with the fingers is to be avoided, but loose necrotic tissue should be removed if it can be done without injury to surrounding structures. The incision and its surroundings are then carefully washed with one of the solutions mentioned, and an aseptic drainage-tube inserted. The wound is dusted with iodoform or dermatol, and an antiseptic dressing is applied, exerting slight pressure with bandage. If the abscess is deep, the drainage-tube should be shortened daily; if it is superficial, the drainage-tube can be withdrawn the second or third day.

Drainage by means of rubber drainage-tubes of sufficient size is preferred to the use of gauze. Two tubes placed side by side facilitate irrigation when necessary.

> The necessity for radical treatment of any local suppurative process which persists in spite of conservative treatment is emphasized by the writer.
>
> Such a suppuration is in numerous instances a grave menace to the body.
>
> Tubular drainage should be used only when a suppurating cavity is to be drained, when it is impossible to make a large opening, or when the drain cannot be safely inserted at the lowest point.
>
> The introduction of gauze into a suppurating cavity insufficiently opened is a blind and dangerous procedure.
>
> The best method of determining how and where gauze should be inserted is to introduce a gloved finger. D. Taddei (Riforma med., xxxvi, 447, 1920).

When it is necessary to traverse the peritoneal or pleural cavity in order to reach a collection of pus, infection may be avoided by carefully packing off the cavity with gauze, so as to form a sort of well with the abscess at the bottom.

The kind of dressing used after the abscess has been opened will depend upon the condition of the parts. If there be much infiltration of the tissues, swelling, and pain, a hot, moist antiseptic dressing is to be applied, as it favors absorption and is at the same time soothing to the patient. Any weak antiseptic solution (barring carbolic acid for fear of gangrene) may be used, as **boric acid, bichloride of mercury** (not stronger than 1 to 20,-000), or **normal salt solution.** The dressings (wet or dry) while sufficiently firm to favor collapse and adhesion of abscess walls should yet

be loose enough to permit of easy absorption and evaporation of discharges.

COLD, OR TUBERCULOUS, ABSCESS.—Symptoms.—These abscesses frequently attain a large size, and last for months without their presence being detected. Besides failing general health, the symptoms of the causative trouble are the only prominent ones. The spine, the hips, the genitourinary tract, and the lymphatic glands are the organs most prone to tuberculous disorders giving rise to cold abscesses. They sometimes appear several months and even years after the beginning of the primary disease.

The *general symptoms* of tuberculous abscesses do not closely resemble those of ordinary suppuration, but vary with the resisting powers of the individual. There is nearly always a slight evening rise in temperature (hectic) followed by a subnormal temperature in the morning. Loss of flesh and strength and the presence of anemia, more or less marked, are usual, although they may not occur unless mixed infection (tubercular and purulent) takes place. There is no leucocytosis. Amyloid (albuminoid) degeneration may appear as a later phenomenon.

The *local symptoms* are as a rule very slight, and are indicative of the effects of pressure upon organs or nerves rather than activity in the abscess itself. Large fluctuating abscesses may exist in various parts of the body, even about joints, without serious discomfort to the patient. No pain is experienced as a rule; cold abscesses are not even tender to the touch. There is no redness until the abscess is about to break, the focus of the liquid mass being otherwise too deeply seated, the skin covering the abscess remaining white or normal in color unless the abscess be just beneath the surface, which phenomenon has caused the name "white swelling" to be applied in tuberculosis of the knee.

The above symptoms usually follow or are coincident with the sudden appearance of a swelling. Though generally soft, it may be hard, and suggest a tumor in the vicinity of the spinal column (Pott's disease), above or below Poupart's ligament, after burrowing along the psoas muscle (psoas abscess), on the inner aspect of the thigh, or in the lumbar region (lumbar abscess), etc. In the neck cold abscesses are usually due to disease of the neighboring cervical lymphatic glands. The skin either remains normal or gradually becomes thinned and softened until an external opening is formed.

Fluctuation, usually detected with ease, is sometimes hidden by a thick investing layer of lymph, which gives the mass a peculiar tension, suggesting a lipoma or some other hard growth. Aneurisms sometimes convey the sensation produced by a cold abscess: a fact to be borne in mind when operative procedures are under consideration.

Pathology.—A cold abscess can always be traced to a specific inflammatory process, and almost invariably to one of a tubercular nature. Where the confluent masses in the center of a nodule begin to break down, there is formed a collection of material surrounded by tuberculous tissue. This material becomes infiltrated with leucocytes, and thus is produced a cavity containing fluid fatty material, frag-

ments of cells, and leucocytes, around which there is granulation tissue filled with tubercles. In this way a tuberculous abscess is formed. It seems at times to be quite a matter of accident whether the abscess breaks into the joint or finds its way by a more circuitous route into the surrounding connective tissue. As the tuberculous masses spread, caseation takes place at different points in the wall, and the masses are discharged into the cavity of the abscess; but the spread of the abscess is effected generally by what is termed "burrowing of pus." This burrowing occurs in various directions, and large collections of pus altogether out of proportion to the original lesion are formed, and are known as cold abscesses.

What has been called a chronic abscess is very often no abscess at all. In tubercular processes the product of tissue proliferation undergoes coagulation necrosis, and disintegrates into a granular mass, which, when mixed with a sufficient quantity of serum, forms an emulsion that microscopically resembles pus, but under the microscope shows none of the histological elements which are found in true pus. An abscess can only be called such if it contains pus. A true chronic abscess can originate in a tubercular, actinomycotic, or syphilitic lesion, when the granulation tissue is secondarily infected by the localization of pus-microbes, which convert the embryonal cells into pus-corpuscles.

Differential Diagnosis.—The concomitant disorder usually makes a diagnosis easy in a case of cold abscess; but occasionally the swelling is the only indication of ill health, and it is important to determine, under such circumstances, the nature of the pus. The macroscopical appearances of "laudable" pus and of "sanious" pus are frequently so similar that a *de visu* diagnosis is not justified. Bacteriological examination of the contents of such abscesses will show conclusively whether they are true pus-containing abscesses or whether or not they are pseudo-abscesses. If cultivations are made of their contents, pus-microbes will grow upon proper nutrient media if it be a true abscess, while from the contents of a pseudo-abscess only the microbes of the primary infection can be cultivated. The information obtained by the discovery of the essential cause can be confirmed by inoculation experiments.

Prognosis.—The walls of cold abscesses are usually tense and tough, and are lined with cheesy tuberculous material. They do not tend to collapse, as is the case with acute abscesses, and for that reason are healed with difficulty. When, however, the seat of the original trouble can be reached and successfully treated, the fluid in the parts of the abscess tract is absorbed, and the caseous matter undergoes calcification. This fortunate issue of the case is seldom met with, however, and the abscess usually continues, the primary etiological factor acting as a drain for the diseased area. The prognosis, therefore, depends upon the result obtained in the treatment of the latter.

Surgical Treatment. — Experience has shown that when such a cold, or tuberculous, abscess opens spontaneously, or is incised in a careless way, profuse suppuration and hectic fever follow, with only too often a speedy fatal result from septic infection.

Unless the surroundings of the patient admit of carrying out the antiseptic treatment to its full and perfect extent, a chronic abscess should not be evacuated by incision. It should be aspirated.

> Incision of a cold abscess dooms it to infection with all of the dire consequences from chronic sinuses through amyloid disease to death. Even retropharyngeal abscesses should be drained only through aspiration. In very chronic cold abscesses cure is not infrequently possible as a result of repeated **puncture** and complete **aspiration** with suction. E. A. Rich (N. W. Med., July, 1916).

Our associate editor, Prof. Robert T. Morris, of New York, referring to tuberculous glands of the neck (see also Adenitis, this Index), called attention two years ago to the fact that in the large number of cases treated by him in the New York Post-Graduate Hospital in recent years, he had only resorted to operation those abscesses that were actually suppurating. All others were treated conservatively to avoid general infection, including miliary tuberculosis. In a number of cases the use of the new high-penetrating **X-ray** proved most effective. More recently he has added **tuberculin** to the other resources, and is convinced that when this method is applied in the right way and for a sufficient length of time it is one of our most important resources against tuberculosis of any kind.

> Evacuation of abscesses of tuberculous nature by incision should never be done; **aspiration** and **injection** of these **abscesses** is at the present time the preferable course to pursue. The injection fluid consists of:
>
> Olive oil .... ℥iiss (75 c.c.).
> Ether ..:........... ℥i-¼ (37 c.c.).
> Creosote .... ℨiss (6 c.c.).
> Guaiacol .... gr. xv (1 Gm.).
> Iodoform .... ℨiiss (10 Gm.).

Of this mixture, ¼ to 1 ounce (7½ to 30 c.c.) is injected, depending upon the age of the patient and the size of the abscess. The abscess is as-

pirated and injected every 10 days 6 times. For fistulas and sinuses the following paste is used:

> Camphorated phenol,
> Camphorated naph-
>   thol, of each .... ℨiss (45 c.c.).
> Guaiacol .... ℨiiiss (105 c.c.).
> Iodoform ....:... ℨv (20 Gm.).
> Creosote .... ℨij (8 c.c.).
> Lanolin,
> Spermaceti, of each. ℨxiij (50 Gm.).

> The sinuses are injected every seventh day and a large sized urethral glass syringe is used. The sinuses communicating are held closed until the paste is solidified. C. W. Delany (Penna. Med. Jour., July, 1917).

On general principles, necrosed or detached bone should be looked for in all cases. Strict antiseptic precautions are imperative to avoid mixed infection (bacilli of tuberculosis and pyogenic cocci). Preliminary precautions should be taken to meet violent hemorrhage due to vascular erosion.

When there is local inflammation and spontaneous opening of the abscess is probable, there should be a free incision, a thorough scraping of its walls with Volkmann's curette to transform the suppurating surfaces into bleeding ones. The cavity is then cleansed with a 5 per cent. solution of **carbolic acid,** a long drain is applied, and the wound is stitched as far as the drain. An antiseptic dressing is then applied. (Volkmann, Trélat, Pozzi.)

After opening the abscess the cavity may be washed out with **peroxide of hydrogen** in 10 per cent. solution or packed with **iodoform gauze.** Removal of the limiting sac is then performed by **decortication,** the steps being: free incision, the sac detached with finger or spatula and removal, and the cavity closed immediately. (Lannelongue.)

The removal of the limiting sac is facilitated by filling the wound with

paraffin; the mass can then be removed as if it were a lipoma. (Cazin.)

A psoas abscess should be opened in the loin and groin when possible. In the loin the incision should be made through the external and internal oblique, transversalis, and lumbar fascia, along the outer edge of the erector spine to the edge of the quadratus lumborum. The latter muscle and the transversalis fascia are divided on a level with the tip of the second or third lumbar transverse process, avoiding the lumbar arteries. The sheath and the psoas are then perforated with the finger or a trocar. A counteropening is then made below Poupart's ligament to form a tunnel, into which a large-size drainage-tube is inserted. This is replaced, later on, by a tube at each end to obtain obliteration, beginning from the center of the canal. If one incision is preferred the loin should be selected.

Aspiration and Injections. — When no local inflammation indicates that the abscess is soon to open, the fluid may be withdrawn with a large aspirator; a 5 per cent. solution of **carbolic acid** is injected and then aspirated. This procedure is renewed until the solution withdrawn is perfectly clear. A Lister bandage is then applied, insuring slight pressure. Five days later the treatment is renewed. About five sittings are required.

Injection fluids: **Iodoform**, 1 part; **ether**, 5 parts; **distilled water**, 5 parts. Injection not to be renewed while iodoform is being excreted in the urine.

Less painful is a mixture of 1 part of **iodoform** to 10 of **glycerin** (Billroth) or of **olive oil** (Bruns).

Intoxication may be prevented by sterilizing the iodoform and excipient (except ether) by heating at 212° F. separately.

Boric acid, a 4 per cent. solution, may be used as above (Ménard), or **naphthol** and **camphor,** 1 part each. About thirty sittings are usually required.

The lesion being a tuberculous one, the general system should be treated accordingly. **Nutritious food,** including a free supply of milk and eggs, **pure air, sunlight,** and **sea-air,** if possible, are indicated, as well as **tonics** and **alteratives** (**codliver oil** and **hypophosphites, iodine, iodides, arsenic, quinine, strychnine,** etc.).

C. SUMNER WITHERSTINE,
Philadelphia.

A. C. E. MIXTURE. See CHLOROFORM.

ACETANILIDE. — *Acetanilidum,* formerly known under the name of *antifebrine,* is obtained by boiling aniline with glacial acetic acid. It is the monacetyl derivative [$C_6H_5.NH.CH_3CO$] of aniline.

PROPERTIES. — Acetanilide occurs as a white or colorless shining powder or as crystalline laminæ. It is odorless, but has a slightly burning and bitter taste.

DOSE. — The dose of acetanilide is 3 to 5 grains (0.2 to 0.325 Gm.) in adults; the tendency, however, is to employ smaller quantities. In children, according to Griffith, the coaltar products of this class are well borne; ¼ to ½ grain (0.016 to 0.033 Gm.) may be given at 6 months, increasing the dose by ¼ grain with each year, until the adult dose is reached. The action of acetanilide should be closely watched in weak subjects and in hysterical women.

Out of 274 observers who stated that they used acetanilide, 17, or 6.2 per cent., employed less than 2 grains as a minimum dose for adults; 113, or 41.2 per cent., employed 2.5 grains or less as a

minimum dose, and 155, or 56.5 per cent., employed from 3 to 5 grains as a minimum dose. Two hundred and forty, or a little over 87.5 per cent., never exceeded a dose of 5 grains, and 34, or not quite 12.5 per cent., employed doses exceeding 5 grains.

An examination of a number of prescriptions for adults on file in various pharmacies in Washington, D. C., brought into court as evidence, showed the average dose of acetanilide prescribed was 2.43 grains. Kebler, Morgan and Rupp (U. S. Dept. of Agricul., Bureau of Chemistry, Bulletin No. 126, July 3, 1909).

MODES OF ADMINISTRATION.

Acetanilide is insoluble in glycerin, slightly soluble in water (1 grain in 3 fluidrams of cold, and 1 grain in 18 minims of hot, water), but completely so in alcohol (1 grain in 2½ minims), and readily in ether (1 grain in 18 minims). It is readily suspended in syrupy mixtures and can be given with most drugs thus administered. Acetanilide is also dispensed by druggists in the form of tablets, which are quite tasteless when taken with a mouthful of water. It may be given in the form of powders or in dilute alcoholic solutions.

There was also formerly official the compound acetanilide powder (*pulvis acetanilidi compositus*), containing acetanilide, 7 parts; caffeine, 1 part, and sodium bicarbonate (to increase the solubility of the acetanilide), 2 parts, the dose of which is 5 to 10 grains (0.3 to 0.6 Gm.).

While acetanilide is not soluble and is readily suspended in syrupy mixtures, it can be combined with ammonia in any of its forms, salicylic acid, nux vomica, digitalis, codeine, creosote, potassium bromide, etc. A prescription can therefore be elaborated that can be much more accurately adapted to the case in hand than any of the ready-made combinations. The foundation of most of the coal-tar product combinations is acetanilide, which has been combined with bicarbonate of soda, caffeine, carbonate of ammonia, etc. The combination may be chemical or mechanical, it matters little which, as it is practically broken up in the body into acetanilide radicals and other constituents. L. Faugères Bishop (Med. News, June 10, 1899).

Various combinations of acetanilide with other drugs (adjuvants and corrigents) may be made to meet the exigencies of practice, some of which are as follows:—

R Acetanilidi .... gr. xij (0.800).
Caffeinæ citratæ .... gr. iij (0.200).
Camphoræ monobrom. .... gr. vj (0.400).
Misce et fiant capsulæ no. vj.

NOTE.—The caffeine and camphor are used as corrigents to the acetanilide.

R Acetanilidi .... gr. xv (1.000).
Sodii bicarbonatis .. gr. x (0.650).
Ammonii carbonatis. gr. xv (1.000).
Misce et fiant capsulæ (not pulveres) no. x.

NOTE.—The sodium bicarbonate aids in the assimilation of the acetanilide, while the ammonium carbonate acts as a corrigent.

R Acetanilidi .... gr. xx (1.300).
Sodii bicarbonatis. gr. xv (1.000).
Caffeinæ .... gr. vj (0.400).
Acidi citrici .... gr. x (0.650).
Misce et fiant capsulæ (not pulveres) no. x.

NOTE.—The caffeine and citric acid in the above should be mixed and slightly moistened; this allows the formation of a fresh preparation of citrated caffeine; it should then be dried and mixed with the other ingredients.

R Acetanilidi .... gr. xx (1.300).
Sodii bicarbonatis. gr. xx (1.300).
Sodii salicylatis . ʒiss (6.000).
Misce et fiant chartulæ no. x.

NOTE.—The sodium salicylate is used as a synergist to the acetanilide.

R Acetanilidi .... gr. xx (1.300).
Potassii bromidi . gr. xxx (2.000).
Sacchari lactis .... gr. xv (1.000).
Misce et fiant chartulæ no. vj.

NOTE. — The potassium bromide is used as a synergist to the acetanilide.

℞ *Acetanilidi* .... gr. xxv (1.600).
  Potassii bromidi . gr. xv (1.000).
  Caffeinæ citratæ . gr. v (0.325).
  Misce et fiant capsulæ no. x.

℞ *Acetanilidi* .... gr. xxv (1.600).
  Sodii bicarbonatis. gr. x (0.650).
  Caffeinæ citratæ . gr. vj (0.400).
  Camphoræ mono-
    bromatæ .... gr. vj (0.400).
  Misce et fiant capsulæ no. x.

℞ *Acetanilidi* .... gr. x (0.650).
  Sodii bromidi .... gr. L (3.250).
  Extracti hyoscy-
    ami .... gr. v (0.325).
  Caffeinæ citratæ . gr. v (0.325).
  Morphinæ sulphatis. gr. ⅕ (0.013).
  Misce et fiant tabellæ (or capsulæ)
no. x.

Note.—The sodium bromide, extract of hyoscyamus, and morphine sulphate all act as synergists to the acetanilide, while the caffeine corrects their action.

℞ *Acetanilidi* .... gr. xx (1.300).
  Quininæ sulphatis gr. xx (1.300).
  Extracti hyoscy-
    ami .... gr. v (0.325).
  Extracti cannabis
    Ind. .... gr. iiss (0.163).
  Arseni trioxidi .. gr. ¹⁄₁₀ (0.0065).
  Strychninæ sul-
    phatis .... gr. ⅕ (0.013).
  Misce et fiant tabellæ (or capsulæ)
no. x.

Note.—The strychnine sulphate is used instead of the caffeine as a corrigent.

℞ *Acetanilidi* .... ʒj (4.000).
  Zinci oxidi ...... ʒj (4.000).
  Amyli .....q. s. ad ʒj (32.000).
  Misce et fiat pulvis.
  Sig.: Use as a dusting powder.

℞ *Acetanilidi* .... ʒj (4.000).
  Adipis lanæ .... ʒij (8.000).
  Petrolati ..q. s. ad ʒj (32.000).
  Misce et fiat unguentum.

℞ *Antipyrinæ* .... ʒj (4.000).
  Caffeinæ citratæ .. gr. xx (1.300).
  Aquæ destillatæ . fʒiv (120.000).
  Misce et fiat solutio.
  Sig.: Teaspoonful as required.

Note.—In the above prescription antipyrin is used, as it is very soluble, while acetanilide is almost insoluble. W. H. Foreman and J. H. Gertler (Jour. Indiana State Med. Assoc., June 15, 1909).

It has been supposed that the addition of caffeine to acetanilide decreased its toxicity, and, therefore, the likelihood of untoward effects. Hale has shown experimentally, however, that such was not the case, and, indeed, that it greatly increased it. Sodium bicarbonate, on the other hand, tends to lessen the toxic effects of acetanilide upon the heart.

By experiments on the hearts of warm- and cold- blooded animals the writer found caffeine of little or no benefit in acetanilide poisoning in so far as the cardiac energy and the blood-pressure were concerned, and that it apparently exerts a harmful effect in some cases. But there appeared, especially in the dog, to be a well-established antagonism on the heart rate which, however, would probably be insufficient to be of any value in cases of poisoning in man. Feeding experiments demonstrated the absence of antagonism between acetanilide and caffeine, in all cases the addition of the latter drug causing death more quickly or with a smaller dose. This, in connection with the imperfect antagonism to the heart action, makes the use of caffeine in acetanilide mixtures especially questionable. Sodium bicarbonate, in contrast, lessens the toxicity of acetanilide, both in its action on the heart and on the intact animal, increasing the duration of life or making the use of a larger dose of acetanilide necessary to cause death. Hale (Jour. of Pharmacol. and Exper. Therap., Aug., 1909).

INCOMPATIBLES.— Acetanilide forms insoluble compounds with the bromides and iodides in aqueous solution, and a soft mass on trituration with chloral, carbolic acid, thymol, or resorcinol. According to Blackwood, unexpected and often alarming effects are observed when calomel is given with any coal-tar product.

CONTRAINDICATIONS. — Acetanilide should not be used when the heart is fatty, weak, or enlarged; in blood disorders such as pernicious

anæmia characterized by cell destruction; in phthisis or other exhausting diseases, and in pregnant or nursing women.

PHYSIOLOGICAL ACTION.— As Antipyretic.—In the normal subject, the temperature, according to Nothnagel and Rossbach and most authorities, is lowered only when toxic doses are given. Not so, however, when fever is present. Here a small dose suffices to produce a marked fall. Dujardin-Beaumetz, for example, witnessed a decline of 3° C. (5.4° F.) and cyanosis in a case of typhoid fever in which 7½ grains (0.5 Gm.) had been administered. Manquat states that 1½ to 3 grains (0.1 to 0.2 Gm.) suffice to influence the temperature, acetanilide, according to Krieger, Cahn and Hepp, being far more active in this particular than antipyrine. Sweating and chills are occasionally observed.

The investigations of Hare and Evans suggested that the fall of temperature produced in febrile cases was due to a decreased heat-production and increased heat-dissipation. But Wood, having found that the *rectal* temperature not only did not fall as did that of the surface, but that it rose, concludes that the experiments of Hare and Evans "cannot be used to explain how antifebrin reduces the temperature." Moreover, most European investigators, Lépine, Podanowsky and others, hold that acetanilide acts by depressing the heat-center. According to Cushny, it affects the nervous heat-regulating mechanism in such a manner as to lower the level at which the body-temperature is maintained, the loss of heat necessary to produce the fall in temperature being accomplished by dilatation of the cutaneous vessels. The manner in which acetanilide acts as an antipyretic is stated by Butler to be far from understood.

Action as Analgesic.—According to the prevailing view, acetanilide acts directly as a sedative upon the nervous system, especially upon the sensory portion of the spinal cord; with toxic doses the effect may extend to total loss of reflex action and sensory and motor paralysis, the muscles being influenced only directly. Wood holds that, "directly or indirectly, acetanilide affects the cerebral function," though at a certain stage of its toxic action consciousness may be uninfluenced while the rest of the nervous system is clearly affected. Bokaï ascribes the effects of acetanilide to paralysis of the motor nerve-endings in the muscles, sufficiently prolonged exposure of the latter to the poison also annulling their ability to contract. Cushny, referring to this and other coal-tar products, states that "by many they are supposed to have a sedative or depressant effect on the nervous system." The analgesic action of acetanilide is generally ascribed to this supposed sedative effect, though all agree that applied locally to the tissues it acts as a stimulant or mild irritant. Its toxic effects, however, should not be overlooked.

Action on the Blood.—The cyanosis produced by excessive doses of acetanilide is ascribed by Lépine, Hénocque and others to transformation of the hemoglobin into methemoglobin, and by Vierordt, Halliday and others to the reduced hæmoglobin as it occurs in venous blood. Some contend that the red corpuscles are disorganized, while others hold that they remain intact.

Acetanilide, antipyrin, and acetphe-netidin lower the total amount of oxygen in the circulating arterial blood. The diminution is slight with antipyrin, which, in fact, in large and medium-sized doses causes at first an increase. With the other two agents the decrease is both pronounced and constant. The variations in the amount of carbon dioxide in the blood are not parallel with those in the oxygen. The respiratory functional capacity of the blood and the respiratory interchanges are diminished. Piccinini (Arch. Inter. de Pharm. et de Thérap., vol. xxii, Nos. 1 and 2, Cyclo. Suppl., 1918).

Action on the Circulation.—Injections of acetanilide in animals have been found to cause at first a slight increase in the number and force of the heart-beats, with corresponding rise of blood-pressure. Later, and also from the first with larger doses, circulatory depression is observed. In febrile patients the lowering of temperature produced by the drug is often accompanied by reduction in the frequency and size of the pulse. Large doses are said to depress the heart directly.

[These phenomena are the normal results of the exciting action of the drug upon the sympathetic center and the resulting constriction of the arterioles. Those of the heart admitting less blood into its muscular walls, the force of its contractions and their number are reduced. The heart's action may be arrested by the same process. C. E. DE M. S.]

UNTOWARD EFFECTS AND ACUTE POISONING.—The symptoms of poisoning include primarily the cyanosis, which begins at the lips and then extends, gradually becoming more intense, over the face and the rest of the body, and is accompanied by profuse sweating and prostration. In some cases there is ashen lividity and the temperature falls rapidly to 95° F. or lower. The pupils are dilated and fixed. The respiration is slow and shallow, and the pulse becomes steadily weaker and then irregular and fluttering. Somnolence, unconsciousness and coma, and cardiac arrest follow. In some instances sudden heart-failure occurs soon after the onset of the symptoms, the organ being arrested in diastole. Erythematous or urticarial skin eruptions and disorders of hearing are occasionally observed.

An instructive case was published by Ballou some years ago. The patient was a man, aged 45, suffering from a form of intermittent fever. He complained of almost unbearable headache; pulse, 120; respirations, 23; temperature, 104.8° F. Ten grains of acetanilide were given, and about 20 minutes later the patient said his headache was relieved, and that he felt easier. About 45 minutes after the drug was administered all sweating ceased, and a peculiar sensation of warmth under the skin was complained of. To this, in 12 or 15 minutes, was added intense itching, while in 3 or 4 minutes the whole body presented a general erythematous condition. The entire surface was of a brighter red than that of a typical case of scarlet fever, and, like the scarlatina rash, it disappeared on pressure, to return as soon as pressure was removed. No part of the body was exempt from this rash, the conjunctivæ, palms of the hands and soles of the feet being as red as any part of the body. The temperature of the surface seemed elevated, but the thermometer in the mouth showed that it was gradually falling. The body appeared as if every superficial capillary was dilated.

With the appearance of the rash the itching became more intense, the patient assuming all positions possible while scratching. Within the external ear the itching was especially intense, but there was no disturbance of hearing. The rash lasted for 6 hours, without any apparent change, and then disappeared rapidly from all parts of the body simultaneously, and as the rash faded the itching subsided.

About this time a slight cardiac irregularity became evident, and this lasted for 4 days. The only drug taken before the acetanilide was calomel (about 5 grains).

The 2 unusual symptoms, intense itching and general erythema, were due to excessive dilatation of the arterioles after the true toxic effects had passed off, the violent excitation to which the poison had subjected the sympathetic center having temporarily exhausted it. EDITORS.

According to the writer, study of the cases recorded in the literature and personal cases proves that the ingestion over a considerable period of time of acetanilide or related coal-tar products is productive of a definite symptom-complex which is highly suggestive, if not absolutely diagnostic, of poisoning by this group. The subjective symptoms are: great general weakness, nervous excitability, insomnia, loss of appetite, digestive disturbances, palpitation, dyspnea, numbness and weakness of the extremities, pain in the region of the liver and spleen, and faint attacks. The chief objective symptom is cyanosis, which is often extreme, but usually fluctuating in intensity, accompanied by marked pallor of the mucous surfaces and without clubbing of the fingers.

The blood-changes are quite characteristic, and due to the destructive action of a hemolytic poison circulating in the blood-stream, which produces a secondary anemia variable in degree. The erythrocytes are diminished in number; they often present nucleated forms, show granular stippling, stain poorly, and are variable in size and form There is usually a moderate leucocytosis of the polymorphonuclear variety, and there is often a relative increase of the lymphocytes. The appearance of the blood as it stands upon the finger-tip or the ear is very suggestive; it is either of a bluish-black color or chocolate in appearance. The coloration of the plasma renders the estimation of the hemoglobin quite difficult. Gordinier (Monthly Cyclo. and Med. Bull., Mar., 1912).

Out of 288 practitioners questioned, 219, or 76 per cent., stated that they had observed instances of poisoning following the use of acetanilide. These 219 observers report 614 cases of poisoning, including 17 deaths, i.e., 2.7 per cent. The character of these cases and the doses used were as follows:—

Pneumonia (child....	One-half grain every 2 hours until 2 grains were taken.
Capillary bronchitis (child)	Small doses frequently repeated.
Capillary bronchitis (child)	Small doses frequently repeated.
Typhoid..............	Five grains every 4 hours
Headache.............	About 20 grains.
Headache............	Thirty grains (?).
Headache............	"Orangeine" taken freely
Headache............	Thirteen or fourteen 5-grain doses in 12 hours.
Headache............	Bromoseltzer.
Neuralgia.............	Dose not given.
Neuralgia of heart...	Five 5-grain doses in 5 hours.
Burn.................	Boroacetanilide applied freely.
Burn (infant).........	Acetanilide applied freely to umbilical cord.
Headache............	Excessive doses of "bromo-seltzer."
Typhoid (child)......	Five grains.
Typhoid (child)......	Dose not given.
Malaria (child).......	One and one-half grains.

Kebler, Morgan and Rupp (U. S. Dept. of Agricul., Bureau of Chemistry, Bulletin No. 126, July 3, 1909).

Experiments conducted by the writer to ascertain whether acetanilide appeared in the milk of a nursing mother, and, if so, whether in sufficient quantity to cause the death of an infant. They showed that acetanilide derivatives are at times eliminated, but that more frequently there is no trace of them in the maternal milk or the infant's urine. The quantity found in each case was so minute that it could only be detected by holding the specimen against a white background. The time of the first appearance of the reaction after the administration of a dose of 4 grains varied from 7 to 15 hours. Stevenson (Mich. State Med. Soc. Jour., Apr., 1914).

The great majority of such cases are due to intoxication by proprietary headache powders sold under a vari-

ety of fancy names. Proprietary preparations containing acetanilide were reported to have been used in 77, or 12.5 per cent., of the 614 cases of poisoning mentioned above by Kebler, Morgan, and Rupp. It is well known that certain individuals show an idiosyncrasy to the drug, and in some instances very small doses will suffice to cause death.

Many instances of "headache powder" victims have been published. Philip Brown, for instance, observed a case of fatal poisoning from this cause. The patient, a man of 37, had taken six "headache powders" each containing 10 grains. He became delirious, complained of abdominal pain, vomited, and was slightly jaundiced. His temperature rose to 100.2° F. (37.9° C.), the lips and nails became intensely cyanotic, respirations shallow and frequent. The urine, of which 10 ounces were passed on admission, was nearly black and strongly alkaline. Anuria occurred, and 6 days later the man died. There was alternate constipation and diarrhea, and 48 hours before death the feces constantly showed blood-pigment, blood-clots, and corpuscles.

Another case of acetanilide poisoning with fatal results following the ingestion of "bromoseltzer" taken to relieve a headache, was published by Hemenway. The heart, already weakened from repeated doses of the drug, was unable to stand a slight overdose and the victim died in a few hours.

In a case of acetanilide poisoning, observed by Summers, in a woman, aged 26 years, who had taken 8 grains, there occurred collapse with strong convulsive movements, partial loss of consciousness, and great retching. **Whisky, strychnine nitrate,** and—for two hours—**artificial respiration** induced recovery.

In another instance observed by Earps the patient had taken four headache powders. These had been taken each hour between nine and noon. The surface of the body presented an ashen-gray appearance, the mucous membranes having a much darker hue. The temperature was 96 degrees; pulse, 60, and respiration, 10. **Digitalis, strychnine,** and **alcohol baths** with **friction** were employed, with **dry heat** to the surface. When the patient was able to swallow, a combination of **aromatic spirit of ammonia, brandy,** and **capsicum** was given. Twenty-four hours later the temperature was slightly subnormal, the dusky appearance of the face disappeared to a large extent, but the symptoms of cyanosis did not wholly vanish until the second day. The powders contained 3 grains of acetanilide, 2 grains of bicarbonate of sodium, and 1 grain of caffeine; hence the total dose was 12 grains of acetanilide.

The doses capable of producing toxic effects are sometimes very small, but it is probable that some of the drugs recommended in textbooks for the treatment of poisoning by coal-tar products, strychnine and belladonna, for example, do more harm than good, and that small doses may thus prove fatal through the toxicity added to theirs by the supposed antidotes or remedial measures.

When a large dose is taken, the symptoms once started may suddenly assume marked severity.

Case in a man 52 years of age who suffered from severe chronic headache. Not obtaining relief from headache pills and powders he purchased an ounce of acetanilide in bulk and took a half-teaspoonful—about 30 grains. The headache disappeared in a short time, and he then went out on the street. While walking he felt weak. He then went to a barber shop, and the man who shaved him noted that he had a "terrible blueness." He then entered a store, where in a

few minutes he was seen to sway and fall to the floor. He was found in deep syncope, extremely cyanotic, with a feeble and rapid pulse. He was readily resuscitated, but in a few minutes there was another attack of syncope, which was repeated a number of times during the next few hours. He gradually recovered. J. B. Tyrrell (Jour. Amer. Med. Assoc., Mar. 31, 1906).

Poisoning by Absorption.—Acetanilide having been recommended as a dressing for wounds, burns, and superficial injuries in general, many cases of poisoning have occurred owing to the large quantities applied to the lesions, and the ease with which it is absorbed.

Two cases also emphasizing the necessity of caution even when using acetanilide externally, were published by F. T. Stewart. The first case had sustained an extensive burn of the left lower extremity. The raw surface was covered with Thiersch's skin grafts taken from the right leg and thigh. An assistant dressed the right limb. Early the next morning the patient became cyanotic, collapsed, and became unconscious. It was learned that the right leg had been copiously dusted with acetanilide. This drug has no place in aseptic cases, while in septic cases more efficient and less dangerous agents are available.

Menasses observed 2 cases of acetanilide poisoning from absorption from external wounds in children. The first patient was a baby six weeks old who had a troublesome eczema of the buttocks. A powder was applied composed of equal parts of acetanilide and subgallate of bismuth. Twenty-four hours later the skin of the child was markedly cyanotic, the temperature was subnormal, the respirations were feeble and shallow, the pupils were dilated, the heart was rapid and weak, and extremities cold. **Hot applications** were ordered, with the internal administration of **whisky,** and at the end of three days all symptoms of poisoning had disappeared.

The second case was that of a child of two and one-half years who had received a severe scald of the buttocks. A powder composed of equal parts of subnitrate of bismuth and acetanilide was applied, which soon relieved the pain. On the second day the lips, ears, and finger-tips were blue. The symptoms of prostration were present as in the first case, but not to the same degree. The blueness gradually disappeared, and at the end of a week the wound was healed.

Treatment of Acute Acetanilide Poisoning.—The physiological action of acetanilide being but imperfectly known, cases of intoxication by this drug are treated on general principles, *i.e.,* by measures thought to counteract the symptoms. Cardiac, respiratory and vasomotor stimulants are therefore recommended. **Ether,** hypodermically, has been most frequently used. **Belladonna** is regarded as the best drug to fulfill the indications; it tends to equalize the blood-pressure, especially when external heat is applied simultaneously. **Brandy, digitalis, strychnine, aromatic spirits of ammonia** and inhalations of **oxygen** have all been recommended. **Artificial respiration** is a valuable adjuvant to any treatment adopted.

[In the light of my views, the toxic phenomena being all due to excitation of the sympathetic center, agents which depress this center are indicated. *Amyl nitrite* inhalations, sustained by *nitroglycerin* internally or hypodermically, fulfill this rôle. Artificial respiration is important to insure prompt oxygenation of the blood as soon as the circulation is re-established. Warm (110° F.) *saline solution* intravenously, or, in less urgent cases, per rectum, facilitates excretion of the poison and prevents its irritating action on the sympathetic center, thereby hastening recovery.

Contraindicated.—*Digitalis,* which, like acetanilide, though less actively, excites the sympathetic center, and *alcohol,* which, by becoming oxidized in the blood, favors its conversion into venous blood, and, therefore, cyanosis. *Large doses of strychnine,* which, by causing excessive vasocon-

striction, tend to increase the constriction of the arterioles caused by the poison. C. E. de M. S.]

CHRONIC ACETANILIDE POISONING.—The symptoms of this condition are: cyanosis, which may be extreme, anemia, and wasting. The anemia may be of sudden onset and is evidenced by a distinct leucocytosis, marked reduction in the hemoglobin percentage and in the number of red corpuscles, some of which show nuclei. Other common symptoms include disordered digestion, enlargement of the spleen without tenderness, prostration, weak and frequent pulse, dyspnea, excitability, tremor, and mental aberration, with a tendency to deceive in denying the use of the drug. The urine is dark-colored. The combination of warm extremities with marked cyanosis is considered a distinguishing feature of poisoning by acetanilide.

The blood changes above mentioned may not be accompanied by marked impairment of health. Experiments in animals have shown that the prolonged use of acetanilide tends to cause fatty degeneration of the heart, liver, and kidneys.

> Case of a young woman who had persisted in taking some coal-tar product originally prescribed for migraine. About a year after her marriage she died suddenly following an apparently normal labor. The knowledge of the continued use of the prescription during pregnancy gave the clue to the cause of death. A great danger of chronic poisoning with coal-tar products is the sudden yielding of the heart to unusual strain. S. Solis-Cohen (Boston Med. and Surg. Jour., Feb. 22, 1906).
>
> Case of chronic acetanilide poisoning. The patient had long used acetanilide, about a dozen 5-grain tablets in twelve hours. She pro-

cured 1000 at a time, and in four years had used several thousand. She suffered from severe headaches and vomiting attacks lasting for two or three days, and, as a rule, she would have to be in bed. Two years earlier she began the use of morphine together with the acetanilide and was using as much as 2 grains of morphine a day to get relief. When first seen, she had been in bed for six weeks, was emaciated, no appetite on account of persistent vomiting, headache always present; slightly jaundiced, with marked tenderness and dullness over the gall-bladder region; very constipated, and suffering from tympanites. Dr. A. F. Jonas drained the gall-bladder of dark, thick, stringy bile. She made a good recovery from the effects of the operation, and in three weeks was up and around a little. She stopped the use of any drug and in a couple of months was doing her work and feeling well. About a year and a half later suffered from headache, vertigo, faintness, tinnitus, psychic irritability, dyspnea, palpitation, and edema, with tenderness over the gall-bladder region; large quantities of bile and mucous were being vomited. She was using coal-tar products and morphine to relieve the pain. Her lips and finger-nails were blue. She had lost about 20 pounds in weight during 4 to 6 weeks. Overgaard (Western Med. Review, March, 1911).

Recent years have fortunately shown very few cases of acute, or chronic poisoning, both the profession and the public having realized the dangers of acetanilide as an analgesic.

Treatment of Chronic Acetanilide Poisoning—Under the gradual withdrawal of the drug, **strychnine and digitalis,** these cases usually recover promptly. If pains and insomnia occur, **codeine** may be used tentatively lest another evil habit be initiated. Constipation, which is apt to follow for a time, should be counteracted by

saline aperients. Sympathy and encouragement are potent factors for good in these cases.

The acetanilide—and this applies to all coal-tar analgesics—habit is much more easily recovered from than the opium and morphine habits, and offers, therefore, in this respect a marked advantage over the latter.

> Case of a man, aged about 26, under treatment for two years for syphilis, who had taken enormous doses of the iodides. He had suffered greatly from headache and showed an obscure and progressive tendency to cyanosis. The character of the latter, with the cardiac symptoms and splenic enlargement, led to the diagnosis of acetanilide poisoning. It was learned that the patient had had migraine previous to the specific infection and formed the habit of taking various headache powders. Lately he had been using from six to twenty "orangeine" powders daily. Attempts to withdraw the drug being followed by intense headache, small doses of **morphine** were substituted without the patient's knowledge. All the symptoms disappeared and the patient left the hospital without having taken either acetanilide or morphine for two or three weeks and without the knowledge that he had had the latter. The headache did not return. J. C. Wilson (Boston Med. and Surg. Jour., Feb. 22, 1906).

APPLIED THERAPEUTICS OF ACETANILIDE.—There is no ordinary acute febrile state (the temperature remaining below 105.5° F.) in which the use of acetanilide as an antipyretic is warranted. In typhoid fever, for example, it causes, as shown above, and even when given in very small doses, marked depression tending to collapse. It favors in no way the curative process, and the more or less sudden fall produced deprives the clinician of an important danger-signal which points to intestinal hemor-

rhage, and thus prevents the utilization of measures calculated to arrest it. The comfort acetanilide brings to the patient is the treacherous and insidious dulling of all sensations many poisons afford; it may be procured quite as effectively and with benefit to the patient by means of cold baths, cool sponging, etc., by abstracting heat. Acetanilide does not shorten the course of fevers, does not prevent complications nor reduce the mortality. The same reasons that prevail against its use in febrile processes cause acetanilide to be contraindicated in phthisis. It has been used to counteract the afternoon rise of temperature, but the advantage gained is more than offset by the depression produced. Ten grains in divided doses have caused collapse.

Most authorities, however, advocate the use of acetanilide or other antipyretics of the coal-tar series when the temperature is sufficiently high to endanger life, *i.e.,* in **hyperpyrexia.**

It is in the diseases of the nervous system that acetanilide has shown itself most valuable. As an analgesic, especially in cases of **neuralgia** or **neuritis,** or in pain from reflex causes, acetanilide has been of marked benefit. In **sciatica, migraine, intercostal neuralgia, gastralgia,** the pain of **optic neuritis** and **glaucoma,** it has been freely used, and still maintains a well-deserved reputation. It is also effective in the neuralgic pains associated with **herpes zoster.**

> All headaches that are severe or long-continued or of regular recurrence should be carefully studied and the causative disorder treated. The most satisfactory temporary treatment in the author's experience has been the following, varied according to age and other conditions:—

R *Acetanilidi* .... ʒj (4.000).
  Sodii bromidi .... ʒij (8.000).
  Caffeinæ citratæ ..... gr. iv (0.250).
  Elix. guaranæ..q. s. ad ʒij (60.000).

One teaspoonful every three hours for headache. E. M. Alger (Therap. Gaz., Dec., 1903).

The **painful menstruation,** especially in young girls, **ovarian pain** and the circulatory and nervous disturbances occurring at the **menopause** often yield to it. It has been used with benefit in **chorea.**

[The manner in which acetanilide relieves pain in menstrual disorders, etc., is similar to that in neuralgia.

In chorea, it is the hyperemia of the cerebrospinal and muscular systems which underlies the choreic movements that is reduced by acetanilide. This drug sometimes proves a valuable adjuvant, moreover, to remedies addressed to the cause of the disorders. S.]

In the **lightning and girdle pains of tabes,** acetanilide has been found very effective by Lépine, Grasset, Hayem and others. But 10-grain (0.66 Gm.) doses are required. These subdue the suffering in one-half hour and can be renewed when necessary.

[This is produced in the same way, the pains being due mainly to hyperemia of the central and peripheral nervous elements, including the nervi nervorum. C. E. DE M. S.]

In **epilepsy,** acetanilide has, on the whole, not shown itself very useful, except in cases characterized by permanently high vascular tension. At best, however, it serves but to defer the paroxysms. This applies also to **tetanus.**

Vomiting of nervous origin or due to marked gastric irritability occasionally yields to its action. Two grains every hour until 6 grains have been taken usually suffice to arrest this morbid symptom. It gives some relief in **seasickness** in doses of 3 to 5 grains (0.20 to 0.32 Gm.).

In **pertussis,** acetanilide has been found to lessen the paroxysms markedly. It can be given in doses of ¼ to ½ grain (0.016 to 0.032 Gm.) in small children.

Acetanilide has been used with advantage in **influenza.** But, as antipyrine and acetphenetidin are quite as effective and less prone to produce untoward effect, they should be given the preference.

Increased comfort to the patient and occasionally general improvement have been secured by the use of acetanilide in **diabetes mellitus.**

In ordinary **myalgias,** especially lumbago, acetanilide proves sometimes very effective. It relieves not only the pain, but also the stiffness. It has likewise been recommended in **acute articular rheumatism,** especially when the pain and swelling are marked. It should not be given when cardiac complications are present. Doses of 5 grains (0.3 Gm.) not oftener than three times daily usually suffice.

Harnsberger found the drug useful in threatened **abortion** and in **habitual miscarriages.**

The drug is sometimes used internally in the treatment of **coryza.** In **pharyngeal irritation** and inflammation it is effective internally, especially when aided by a gargle of 4 grains (0.25 Gm.) to the ounce (30 c.c.) of water. Insufflations of acetanilide are very useful in **tonsillitis.**

[As these are all catarrhal processes in which hyperemia is the main morbid condition, the mode of action of acetanilide is self-evident. C. E. DE M. S.]

LOCAL USES.—Acetanilide has been employed with benefit in cutaneous disorders, such as **eczema, psori-**

asis, urticaria, and **herpes,** usually in an ointment. It may be used in powder form to dust over the initial lesion of syphilis, **mucous patches,** and **chronic ulcerations,** as well as **chancroids.** It has been employed in injections for the treatment of **urethritis** and **vaginitis.** The proportion of the drug used in ointment or liquid applications is generally from 20 to 40 grains to the ounce. It has been extensively used as an antiseptic and analgesic in **wounds** and **burns** of varying extent, one of its main advantages being lack of odor. It is best used in combination with an equal part of finely divided boric acid.

The *danger* of absorption and poisoning by the drug render its local use unwise, however, in any but minor injuries, and the quantity applied at each dressing should not exceed that of a moderate dose given internally. Poisonous effects from absorption have been observed with especial frequency in infants.

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ACETIC ACID.—Acetic acid

is an organic acid obtained from sugar or wood by distillation, or from ethyl alcohol by oxidation; or again from crude pyroligneous acid. It is also formed normally in the stomach, from sugars and alcohol taken as foods.

PROPERTIES.—Acetic acid is a clear, colorless fluid having a strong pungent odor and an intensely acid corrosive taste. It contains 36 per cent. of glacial acetic acid: a monohydrate presenting the physical properties of acetic acid, which, in turn, becomes crystalline at 34° F.

The *dilute acetic acid* is officially prepared by adding 1 part of acetic acid to 5 of water. Good vinegar corresponds approximately in strength with dilute acetic acid. Each is used as a local astringent, and internally or by inhalation as a stimulant.

Glacial acetic acid is employed as an escharotic. The crystalline form is mainly employed with sulphate of potassium in the preparation of smelling-salts.

Trichloracetic acid prepared by treating acetic acid with chlorine, which occurs in the form of deliquescent crystals, is to be preferred as an escharotic.

USES AND DOSE.—The preparations available are:—

Glacial Acetic Acid *(Acidum Accticum Glaciale)* ; escharotic.

Acetic Acid *(Acidum Aceticum)* ; used externally.

Dilute Acetic Acid *(Acidum Aceticum Dilutum,* 6 per cent.) ; dose, ½ to 1 dram (2 to 4 c.c.).

Trichloracetic Acid *(Acidum Trichloraceticum)*; escharotic.

It is miscible with alcohol or water in all proportions.

PHYSIOLOGICAL ACTION.— Applied to the skin glacial acetic acid caused irritation and pain, and the formation of a vesicle; its local application to mucous membranes is attended by immediate blanching of the cellular elements cauterized. When applied to the skin well diluted, as vinegar, for example, it acts as an astringent and produces cold and pallor of the tissues it touches. Greatly diluted, as a beverage, it quenches thirst. In the blood it combines with the alkaline bases, is transformed into acetates, and then into sodium bicarbonate, and thus acts as a diuretic and diaphoretic.

ACETIC ACID POISONING.—The abuse of vinegar, or vegetables and other foods preserved in this agent, tends to produce anorexia, gastric disorders, diarrhea and emaciation. In toxic doses acetic acid causes intense irritation, owing to its property of effecting a partial solution of albuminous bodies and of dissolving gelatinous tissues. This escharotic action, by manifesting itself upon the mucous membrane of the pharynx and larynx, is liable to cause edema of the glottis: a danger to be at once thought of. The immediate manifestations are severe pain in the mouth, throat, esophagus, and stomach, with retching and vomiting and other symptoms attending violent irritation of the digestive tract. General symptoms then manifest themselves: The heart's action becomes rapid and the pulse extremely weak or imperceptible, the face and extremities being cold and clammy and covered with sweat. In very acute cases, somnolence passes into coma, and death ensues.

In moderately severe cases, there occurs, after the disappearance of the acute symptoms, abundant expectoration of mucous, containing necrosed tissue, and slight fever, due to more or less pyemia. The blood is markedly influenced, as shown by the marked anemia, paleness and distortion of the red corpuscles and other phenomena. Such a case usually recovers.

Treatment of Acetic Acid Poisoning.—Alkalies and demulcents should be employed. The bicarbonate of soda in free solution is an effective remedy. Ordinary soap—one containing an alkali—can be used in solution until an alkaline salt is available. Chalk, lime or even wood ashes may be employed in the absence of an alkaline soap. Milk, white of egg, oil or flaxseed tea are useful to form a coating over the esophagus and stomach.

Case of a girl, aged 19 years, who swallowed a considerable amount of strong acetic acid with suicidal intent. She immediately was seized with violent vomiting and with pain and intense burning in the mouth and pharynx. At the hospital she developed a series of pronounced symptoms, which are interesting in view of the rarity of cases of acetic acid poisoning. There was a frequent and feeble pulse and a slightly elevated temperature, a persistent and violent cough with a very abundant purulent expectoration, a veritable bronchorrhea, and occasionally efforts at vomiting which were not successful. The urine was black and smoky, like that of carbolic acid poisoning, and contained 1 per cent. of albumin. The red blood-disks in the fresh blood were very pale, with little tendency to form rouleaux, and with frequent mulberry-shaped distortion. The serum, when separated, had a distinct reddish tint, showing that the hemoglobin had been dissolved from the cells. The heart-sounds and the apex-beat were very weak. The symptoms gradually disappeared, and the patient was discharged cured. The treatment consisted of stimulation in the shape of injections of caffeine, a milk diet, and the use of pieces of ice and of a tannin gargle for the throat. Special attention called to the changes in the blood, the purulent bronchitis, and the degenerative changes in the myocardium resulting in heart-weakness with danger of cardiac failure. Giordano (Riforma Medica, Jan. 27, 1904).

Excellent results were obtained by the writer from lavage of the stomach preceded by a morphine injection to relieve the shock. The esophagus must be soothed by giving the patient by mouth pure olive oil, 200 Gm. (6½ ounces) in 24 hours, keeping this up for 7 or 8 days if needed, followed later by sweet cream, raw eggs, mucilaginous substances and

butter, and gradually ordinary solid food. Water can be given in the form of rectal injections of **normal salt solution,** 100 or 150 Gm. (3½ or 5 ounces) every 2 hours, or by the drop method. The mouth should be kept clean and rinsed with some antiseptic solution. Of 120 cases of poisoning from various caustic substances thus treated but 1 died. Dillon (Russky Vratch, xiv, No. 29, 1915).

To counteract the general symptoms, **strychnine** or **caffeine** may be used. To relieve the burning sensation in the alimentary canal, **morphine** is sometimes used.

THERAPEUTICS.—As an **antiseptic,** acetic acid is possessed of considerable power. As such it may either be applied locally or its fumes may be inhaled.

Acetic acid is frequently used as a **stimulant.** When inhaled its stimulating effects upon the nervous supply of the nasal mucous membrane causes it to sometimes act rapidly in restoring consciousness after **fainting.** In the same manner it may also arrest **vomiting** and **headaches** of nervous origin.

Acetic acid is useful in many disorders of the skin. As an escharotic it is often used on **corns, warts, condylomata,** and **fungous growths.** The glacial acetic acid should be used for this purpose. For the destruction of **papillomata** and other small growths, the trichloracetic acid is more effective. The neoplasm is first anesthetized with cocaine, and a single crystal of the acid is placed upon it. This produces a white, dry mass which falls off. In **alopecia** it has been used with advantage as a vesicant. When it is extensive the scalp should be shaved and dilute acetic acid with equal parts of chloroform and ether applied. Or Besnier's formula may be employed:—

℞ *Chlorali hydrati* .... 75 grs.
   Ætheris .... 6 drs.
   Acidi acetici cryst....... 15-75 grs.
Misce. These applications are repeated two or three times a week at first, and later at longer intervals.

Between times a stimulating oil—as of eucalyptus and turpentine, of each ½ ounce; crude petroleum and alcohol, of each 1 ounce—is applied. This is to be followed by a thorough massage of the scalp for five minutes by the patient. Once a week, or oftener, the scalp is to be thoroughly shampooed with tincture of green soap (Morrow).

In **rodent ulcer** and **lupus vulgaris** acetic acid is of use. Daily applications of a 75 per cent. solution and subsequent rinsing with water are necessary.

In **sunburn** and the various forms of **dermatitis** dilute acetic acid or vinegar limits greatly the cutaneous hyperemia, the main source of discomfort.

Acute coryza is sometimes arrested by the inhalation of acetic acid. This applies also to **epistaxis;** in persistent cases, a tablespoonful of vinegar in a glassful of water hastens materially the beneficial effect inhalations afford.

Glacial acetic acid is useful in preventing the development of **hay fever** by applications after local anesthesia with a 10 per cent. solution of cocaine to sensitive areas of the nasal mucous membrane twice per week. In practically all cases, however, the applications must be renewed each year. In **hypertrophic rhinitis** it may also be used in the same way; but chromic acid is more effective. In **pharyngitis** and **tonsillitis** gargling with equal parts of vinegar or dilute acetic acid and water sometimes proves very efficient.

In **tuberculous laryngitis** it has given good results in arresting ulceration. The ulcers are first scraped and the acid applied with a laryngeal

applicator. Inhalations of a 2- to 3-per cent. solution three times a day, ten minutes at a time, and continued several weeks, have been recommended by several German observers.

Acetic acid has also been found an excellent adjuvant in the treatment of **pulmonary tuberculosis** and **bronchitis** when used every three hours. A convenient method is to pour about a teaspoonful on a saucer and to place this over a fire. The acid is then inhaled while it is evaporating—about ten minutes. At first it proves irritating, but this soon subsides. It is useful in **night-sweats** applied as a lotion. Vinegar half diluted with water is quite as effective.

Diluted with from one to four parts of water, dilute acetic acid was recommended by Wood in **hematemesis.** It has been recommended by Hayem for **dyspepsia,** especially where the digestive activity is deficient, *i.e.,* in hypopepsia.

It is a good succedaneum for hydrochloric acid in the treatment of **gastric** and **acute** or **chronic intestinal catarrh,** ordinary vinegar, a tablespoonful to half a pint of water, being taken daily. It is indicated in those submitted to a diet rich in carbohydrates and unable to take much exercise. It also controls **summer diarrhea** and **true cholera nostras,** vinegar rapidly and certainly killing the bacillus of cholera. Acetic acid has been found to dissolve **fish-bones** accidentally swallowed.

Inhalations of acetic acid are very effective in the **vomiting of chloroform narcosis,** administered as in the "drop" method of anesthesia, the napkin being held near the nose, but not in contact with the tissues.

Dilute acetic acid or vinegar is efficient as a topical application for **sprains** and **bruises** and reduces greatly the effusion and pain.

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ACETONEMIA.—There is considerable confusion at the present time between acetonemia (due to the presence of acetone bodies, betaoxybutyric acid, aceto-acetic acid and acetone in the blood) and "acidosis," clinicians in general referring to these conditions as if they were identical. So competent an observer as C. G. Kerley (77th Annual Session Amer. Med. Assoc., 1916) mentions cases in which there was a distinct acetonuria, and others in which there was a distinct acidosis. Those which showed acetonuria were children fed with too much milk. Most children of runabout age received too much fat and too much sugar. These show high fever; about 60 or 70 per cent. of them show acetonuria. A small percentage of cases of pneumonia, scarlet fever, and other conditions accompanied by a fever also show acetonuria. In these children the power of assimilation of carbohydrates seems to be held in abeyance and acidosis follows. Howland (*ibid.*) also urged that cases of recurrent vomiting were not due to acidosis, but to acetonuria, which is not acidosis. The latter occurs when there is a diminished alkali reserve, which causes recurrent vomiting only exceptionally. The only symptom of true acidosis is hyperpnea, *i.e.,* the exaggerated breathing of the air-hunger type; it may occur without fever or vomiting. Finally, Moore (Amer. Jour. of Dis. of Children, Sept., 1916) states that many cases of acidosis in infancy and childhood are not accompanied by an increase of acetone bodies in the blood sufficient to account for the severity of the acidosis.

Diagnosis.—The presence of acetone in the blood of *children*—acetonemia—due to fat ingestion is associated, according to Silberstein (Münch. med. Woch., July 23, 1912), with markedly coated tongue, vomiting, pallor, and fever. This syndrome sometimes follows the ingestion of cod-liver oil. Repeated attacks in the same child have been traced to the ingestion of

whipped cream, milk, cheese, etc. A fruity odor of the breath and acetone in the urine usually accompany these attacks.

Fröhlich (Norsk. Mag. f. Laegevidenskaben, Apr., 1916) noted, besides the foregoing symptoms, thirst, oliguria, urticaria, herpes, pains in the joints, pruritus (the two latter also mentioned by J. P. Crozer Griffith), all of which may precede vomiting, mucomembranous colitis (Comby), and tachycardia. The vomiting may last from a few hours to several weeks. Improvement sets in as suddenly as the attack began, acetone being eliminated in large amounts in the breath and urine immediately before, thus proving a connection between the two.

Blodgett (N. Y. Med. Jour., Aug. 28, 1915), referring to cases of contagious disease, accompanied by acetone in the urine, states that in almost all there is a sore spot that can be found on deep pressure over the region of the pancreas. This spot can be distinguished from the abdominal muscular soreness that follows attacks of vomiting by the fact that it is only found on deep pressure, and is only 2 inches in diameter, over the pancreas.

It is difficult at times to distinguish between acute appendicitis and an attack of periodical vomiting with acetonemia. Palpation of the appendiceal region through the rectum is sometimes the only means to clear up the case. The writer advises in case of persisting doubt to remove the appendix. There is always a possibility that the 2 affections may be associated. He reports 3 cases in which the profuse elimination of acetone by the breath and kidneys was accompanied by frequent vomiting and occasional severe diffuse pains in the abdomen, the pulse fast and small, and the children were restless and felt badly, and there was no stool. The abdomen was distended but this was uniform, and no specially tender points could be found. While the surgeon was studying the first case with the internist, all the symptoms suddenly subsided. Guidi (Rivista di Clin. Ped., Oct., 1917).

The writer found a chemical method for estimating quantitatively the acetone in the breath to determine if acetone bodies are present in the body and in what amounts of practical value in many cases, especially in hyperpnea when acidosis is recognized or suspected. In diabetics it affords a rapid quantitative measurement of the amount present; it proves useful in diagnosing diabetic coma, and when coma is impending or changes in diet are being made. When the patient has been getting little or no food, as in fasting or recurrent vomiting, the determinations of the acetone in the breath act as a guide to the patient's condition. The test is briefly as follows: The air for the determination is collected in a rubber bag of 1000 c.c. capacity when full. Within 30 seconds after collecting the specimen, it is blown through the Scott-Wilson acetone reagent. If acetone is present a white cloud is formed which reaches its maximum density in about 5 minutes. Higgins (Johns Hopkins Hosp. Bull., Dec., 1920).

ETIOLOGY.—Referring to the **periodical** vomiting **acetonemia of children**, Fröhlich (*ibid.*) holds that defective utilization of fat as well as of carbohydrates plays some part in the disturbance. Hecker ascribed the greatest share in this periodical acetonemia to retarded development of certain organ-systems or groups of cells which are especially concerned in the digestion of fat, such children being at all times close to the limit of their digesting capacity for fat. Anything that causes them to step over this limit is liable to bring on a reaction, an intoxication, manifested clinically by vomiting, prostration and elimination of acetone.

TREATMENT.—Bucknell (Atlanta Jour.-Rec. of Med., Mar., 1916) deems it an error to state that while the cyclic attack is in progress little can be done to stay it. Many children vomiting for days, till nearly pulseless, may be promptly relieved. Body fluids being rapidly drained while there is inability to take liquids by mouth, **water** should be supplied **by rectum**, or, if diarrhea exists, by **hypodermoclysis**. If the stomach contains irritating

substances, it should be washed out with sodium carbonate solution. The colon should also be irrigated, and a solution of sodium bicarbonate given per rectum, to be retained if possible. To depress the vomiting reflex, bromides and chloral hydrate may be used by rectum, though chloretone gave the writer better results. Where vomiting is not too severe, a solution of chloretone (1½ grains—0.1 Gm.—a few drops at a time, in a child about one year old) may be given by mouth, or through a stomach-tube, after stomach washing with sodium bicarbonate solution. To make up for the deficiency of carbohydrates 4 to 8 ounces (120 to 240 c.c.) of a 5 per cent. solution of dextrose should be administered, by rectum, in alternation with sodium bicarbonate solution already mentioned. After a few hours of treatment, vomiting usually ceases. If it recurs, the enemas are to be repeated. As soon as the vomiting has ceased and a cathartic, such as calomel and milk of magnesia, has, if necessary, been given, feeding may be resumed.

Fenner (N. O. Med. and Surg. Jour., Nov., 1914) considers it worth while to try the effect of fractional doses of calomel in the beginning. Soda is usually vomited, particularly if given in the large doses indorsed by so many authorities. At best, except in very weak solution, it is a nauseous dose. If frequently repeated it becomes a positive irritant. He has seen children of 2 to 2½ years of age, who could retain their food, such as condensed milk, but who would begin to retch the moment the nurse approached with the dose of soda. Yet the soda was continued.

The sovereign remedy for these cases, in his opinion, of vomiting is morphine. It may be given hypodermically, or in the milder cases by mouth, in very small doses, combined with a tiny dose of cocaine, and a few grains of magnesia in a little chloroform water or plain water. Once the vomiting has been arrested, one may attempt to neutralize the acid condition with alkalies. The agonizing thirst and the dehydration of the tissues are met by the Murphy drip. During the slumber or drowsiness produced by the morphine, the rectal tube can be slipped in without arousing any protest from the baby.   S.

ACETONURIA. — Acetone (C_3H_6O = dimethylketone = CH_3—CO—CH_3) is a thin, watery, very mobile, colorless liquid of neutral reaction. It has a curious aromatic odor, resembling somewhat that of acetic ether or of oil of peppermint. It is soluble in water, in alcohol and ether in all proportions; evaporates at ordinary temperatures; boils at 56.3° C., and has a specific gravity of 0.81. Acetone can be obtained by the distillation of acetate of barium. Oxidation of acetone causes the formation of acetic acid and formic acid. As a product of metabolism, it was discovered by Petters, in 1857, in the urine of a diabetic patient.

Acetone is found in the urine of healthy individuals in quantities not exceeding 10 mg. per day, which, during starvation (Müller), can increase to 780 mg. per day. In some diseases it increases to 0.2 to 0.5 gram daily. By distilling the urine examined, acetone can be obtained in a purer state, although still united with other volatile constituents of the urine.

PHYSIOLOGICAL AND PATHOLOGICAL EXCRETION OF ACETONE. — Pathological acetonuria is observed (1) in high febrile states; (2) in diabetes, especially in advanced cases; (3) in some forms of carcinoma which have not as yet induced inanition; (4) in psychoses; (5) in autointoxication; (6) in functional insufficiency of the pancreas; (7) during the excessive use of animal foods, and (8) in different disorders of the digestion. Lorenz observed acetonuria and excretion of acetone with the feces and the vomited matter in a case of peritonitis. In fever acetonuria is constantly observed, and in the fevers of children as well (Ba-

ginsky). In cases of diabetes, acetonuria occurs when the disease has continued for a long time, and especially when the patients are put on an exclusive diet of proteids or proteids and fat, or when the allowance of food is not sufficient to maintain the equilibrium of metabolism.

In fevers, as well as in diabetes, acetonuria is often accompanied by excretion of diacetic acid and beta-oxybutyric acid.

Five cases of gastric disturbances accompanied by elimination of acetone and acetic acid; the breath had the peculiar odor of acetone at times. Only a few of the children had fever during these attacks. The children were between 3 and 11 years old. The writer ascribes the vomiting to efforts at elimination. Hecker (Münch. med. Woch., July 14, 1908).

Case of periodical vomiting and acetonuria in a child. The patient was a boy of about 3, much depressed by the periodical vomiting. The odor of acetone permeated the air of the room. He had seven attacks of the recurring vomiting, each accompanied by much acetonuria, during the two years afterward, but then he seemed to outgrow the tendency and is now an apparently healthy child. Adenoid vegetations had been removed in the interim. Bloch (Hospitalstidende, June 8, 1910).

A temporary appearance of considerable amounts of acetone bodies in the urine may be due to abnormal and irregular fermentation of sugars and starches in the intestine. They are absorbed therefrom to be excreted in the urine. These bodies are probably not very toxic *per se*, the serious general disturbance of cellular metabolism in diabetes with acidosis being the cause of the gravity of the symptoms rather than the presence in the circulation of the acetone. Derham (Lancet, July 31, 1915).

Not only are acetonuria and acidosis not synonymous, but in the overwhelming majority of cases of *acetonuria*, acidosis is absent (see ACIDOSIS, farther on in this volume). Acetone bodies may appear in the urine in considerable quantity without producing any disturbance. Acidosis, therefore, has come to mean the disturbance which results from a relative excess of acid radicals of any kind in the body, rather than the detection of one or more acids in the urine. If a moderate amount of diacetic acid is formed it is neutralized and excreted in the urine. It is only with an excess of acid that the alkali reserve is diminished. Even then, though there is acidosis, there is no acetonuria unless the acids in excess are those of the acetone series. There is no justification for believing that acidosis due to the acetone bodies occurs in epidemic form. Deficient food or increased requirement for food (disproportion between caloric intake and output) is the chief cause of acetonuria, but this rarely results in acidosis. The production of acetone bodies occurs at times when starvation cannot be held responsible, and is sufficient to cause a severe or fatal acidosis, not necessarily accompanied by vomiting. This condition probably depends on the same underlying metabolic disturbance as do the majority of cases of recurrent vomiting. Howland and Marriott (Amer. Jour. Dis. of Child., Nov., 1916).

It occurs also in association with typhus, pneumonia, variola, scarlet fever, perityphlitis, Bright's disease and strangulated hernia, but it does not lead in such cases to diabetic coma.

Costa found during the last month of physiological pregnancy and in the puerperium (after the eighth day) a more marked acetonuria than in the non-pregnant state. In labor the acetonuria increases. Acetonuria cannot be regarded as a sign of fetal death.

ORIGIN AND PATHOLOGICAL SIGNIFICANCE OF ACETONE, DIACETIC ACID, AND BETA-OXYBUTYRIC ACID.—The origin of acetone in the organism has not yet been ascertained. Cantani was of the opinion that it was formed in functional disorders of the digestive tract; Petters and Kaulich argued that it was due to fermentations in the bowels. Markownikoff ascribed it to a fermentative product of sugar.

Albertoni did not find acetone in the urine of animals which had received large doses of glucose (100 grams) or of different primary saturated alcohol; when isopropylalcohol was ingested it was excreted partly unaltered and partly changed to acetone, and when acetone was given to animals it was discharged by the urine, even if the dose of acetone ingested did not exceed 8 cg.

When Gerhard detected the presence in the urine of a substance which gave a dark wine-red color by means of a solution of perchloride of iron, he believed this substance to be diacetic ether, and was of the opinion that acetone was derived from this substance, which can easily be disintegrated into acetone, alcohol, and carbonic acid.

Fleischer and Tollens then demonstrated that Gerhard's view was erroneous, and found that the coloring substance—at least in the majority of cases—must be diacetic acid, which can be separated from the urine by the addition of sulphuric acid and extracted with ether. This opinion is supported by von Jaksch. Minkowski caused acetonuria by extirpation of the pancreas, and von Mering by intoxication with phloridzin.

Lustig found that extirpation of the solar plexus in animals provoked acetonuria, glycosuria, and emaciation, while Oddi obtained the same results by sugar injections.

Lorenz is of the opinion that diacetic acid and the beta-oxybutyric acid are the substances from which acetone is derived, and that they are the real causes of the toxic symptoms observed in acetonuria, while acetone itself is relatively innocuous.

According to Geelmuyden, the necessary condition for the production of acetonuria is an insufficient decomposition of carbohydrates; he thinks it probable that the bodies of the acetone series are formed in considerable quantity in the organism, to disappear later.

Hubbard found acetonuria more frequent than is generally believed. Its presence without symptoms should not influence operative treatment or prognosis. While its presence with moderate symptoms is of but slight importance, its presence with severe symptoms renders the prognosis very grave.

Von Engel found a great quantity of acetone in the urine of a patient suffering from lactosuria; when the milk was removed by a sucking apparatus the acetonuria disappeared. Very much acetone was found in the urine of patients suffering from severe chronic morphinism. In different acute fevers acetonuria is rather a constant symptom; in typhoid fever von Engel found it constantly; acetone was only missed when the typhoid fever was accompanied by obstipation.

Becker found that acetonuria increased after narcosis, the case being the same with an already existing acetonuria. This would seem to explain why acetonuria has been observed after great operations.

Etherization itself will produce acetonuria in a certain number of cases,

but it also seems very probable that there are a good many other contributing factors which must be taken into consideration, such, for example, as prolonged starvation before and after operation. In a large series of observations made in a children's hospital it was found that boys were more subject to postanesthetic acetonuria than girls. The length of the anesthesia, the amount administered, and the duration of the operation seem to play no part in the duration and severity of the symptoms, but the method of administration of the ether seems to be of considerable importance, as a comparison of figures will show. In 120 cases etherized by the "cone method," acetone was found in 88.5 per cent., while, in the same number of cases in which the drop method was used, only 26 per cent. showed acetonuria. It seems logical, therefore, to consider the "drop method" the best. Hamblen (Univ. of Penna. Med. Bull., June, 1909).

Beesly, Longo, Young and Williams found postoperative acetonuria a quite common occurrence (70 per cent.). The condition is transient, lasting only from two to eight days (Young and Williams). Acetonuria has no influence upon the course of the recovery. Beesly holds that acetonuria due to chloroform anesthesia is more harmful than that caused by ether anesthesia, because ether is less injurious to the hepatic and renal cells and thus does not inhibit their power to carry on their eliminative functions.

The usual risks of anesthesia are not increased by pre-existent chronic acetonuria, but anesthesia (especially by chloroform) may be dangerous with pre-existent acute acetonuria.

The writers have made some observations in 52 cases, of whom only 2, or about 3.8 per cent., had acetonuria before operation, while following laparotomy acetone was found in the urine of 27, or about 52 per cent. The reaction lasted in different cases from two to

eight days. Of the 2 patients whose urine contained acetone before operation, 1 was a colored girl, 15 years of age, who was operated upon for adhesions following an acute attack of pelvic inflammation. The operation was short and the convalescence excellent. Young and Williams (Boston Med. and Surg. Jour., Jan. 23, 1908).

Acetone occasionally accompanied by diacetic acid was eliminated in the urine of 182 out of 214 consecutive surgical patients observed by the writer. They were eliminated oftener and in larger quantities in women than in men. The severity of the operation and the amount of obvious shock had but little bearing on the amount of eliminated acid and the time of elimination. The more emotional, frightened, or anxious individuals invariably were more shocked, and also showed more acetone. Bradner and Reimann (Amer. Jour. Med. Sci., Nov., 1915).

Acetone, diacetic acid, and beta-oxybutyric acid are found in great quantities in the urine of diabetic coma, and different authors—Munser and Strassez, for instance—believe these substances to be the real cause of coma, perhaps by causing an excess of acidity in the organism.

In comatose patients who do not suffer from diabetes—as, for instance, in saturnine encephalopathies, etc.—diacetic acid is often found in the urine. Von Jaksch has proposed to give the name of "coma diaceticum" to these cases of coma. Nevertheless, neither acetone nor diacetic acid and oxybutyric acid have very prominent poisonous properties. Kussmaul gave animals 6 grams of acetone per day without effect. Buhl, Tappeiner, and Frerichs came to similar results. Albertoni found the lethal dose of acetone for dogs to be about 6 to 8 grams per kilogram of the dog's weight.

Geelmuyden draws the conclusion from many experiments on rabbits that, even when small (10 to 20 mg.) subcutaneous injections of acetone are given, the acetone is excreted with the urine; in larger doses more acetone is excreted; but only a portion of the injected quantity reappears; another portion of it is excreted with the expired air; but still a portion is left which does not reappear and must therefore have been disintegrated in the body of the animal. After the injections albuminuria takes place. An adult rabbit can bear an injection of 2 grams of acetone, but is killed by the injection of 6 grams. In starving animals the experiments gave the same results; a portion of the injected acetone reappeared in the urine and the expired air, while still another portion was disintegrated in the body. Geelmuyden draws from these experiments the conclusion that the acetonuria observed in starving individuals is not caused by a diminution of the power to disintegrate acetone already formed in the body, but to an increase of the amount of acetone formed in the body.

Modern authors generally admit that acetone is a product of the metabolism of proteids. Hönigmann and von Noorden are of the opinion that acetone is only formed by diminution of the organized albumin of the body, and never by the metabolism of the proteids ingested with the food, be the quantity ever so large. Hönigmann supported this theory principally by experiments made on himself, which proved that when he lived exclusively on large quantities of proteids—that is, when nutrition was insufficient—acetone and diacetic acid were found. The acetonuria was not augmented when more albumin was ingested, but disappeared when he took plenty of carbohydrates in addition to the proteids. Von Engel, on the contrary, is of the opinion that in all cases when great quantities of albumin are decomposed in the body the quantity of acetone excreted with the urine will increase considerably,— equally if the albumin is ingested with the food or taken from the stock of the body.

Weintraub and Hirschfeld are decided opponents of this theory. Weintraub argues that—in a case of severe diabetes where complete equilibrium of the metabolism, and especially of the metabolism of nitrogen, was maintained for a long time, so that no albumin contained in the tissues was consumed—acetone, diacetic acid, and beta-oxybutyric acid were constantly excreted with the urine; the diet was free from carbohydrates; when, also, the quantity of proteids was somewhat reduced the sugar disappeared after twenty-four hours; the weight of the body was maintained, but acetone and diacetic acid were still excreted (Magnus-Levy).

Carbonate of soda augmented the quantity of acetone excreted, without diminishing the quantity of oxybutyric acids. When, in periods of twenty-four hours, no food at all was taken, acetonuria was greatly increased. Ingestion of carbohydrates diminished the acetonuria, even in persons suffering from diabetes; levulose, milk, and sugar have the same property; glycerin, also, as observed by Hirschfeld. The addition of fat to the food has no power to arrest the acetonuria.

Hirschfeld found that when he put two individuals on light diet, consist-

ing only of proteids and fat, diminution of albumin of the body, as well as acetonuria, was produced. When carbohydrates were added to the food the acetonuria diminished, and that to a much greater degree than the diminution of albumin. Ingestions of fat had absolutely no influence in diminishing acetonuria, although it diminished the loss of nitrogen. Acetonuria is more marked when the albuminous food is scarce than when it is given in great quantities. The ingestion of carbohydrates has an extraordinarily rapid effect on the production of acetonuria, the quantity of acetone being considerable within two hours.

Experiments in persons who were almost starving have proved that a moderate quantity of carbohydrates was sufficient to bring about marked diminution of acetonuria in spite of the considerable loss of albumin and fat which still took place.

Geelmuyden, from his experiments on rabbits and dogs already mentioned, reached the conclusion that acetone is formed in the tissues, not in the kidneys; that the kidneys give passage to the acetone, even when their blood contains a very small quantity of it, and that pathological acetonuria is not caused by a defect of disintegration of acetone in the body, but by a disorder of the general metabolism leading to the formation of an anomalous large quantity of acetone. Geelmuyden has further conducted a series of experiments in healthy individuals (medical students) put on different scales of diet, which were strictly controlled. As all observers did, Geelmuyden found that when a person was put on exclusive flesh diet acetonuria appeared,

and at the same time the body lost albumin as well as fat; when large quantities of proteids were ingested, acetonuria was less considerable than when less albumin was given. Complete starvation, an exclusive fat diet, and a diet of proteids, with the addition of a great quantity of fat, cause a very considerable amount of acetone to be excreted. As exclusive diet of fat and complete starvation give rise to the excretion of the largest quantity of acetone, it seems that acetone is formed by disintegration of fat, and that in this respect there is no difference between the fat of the food and that of the tissues. Carbohydrates have a great power to check the excretions of acetone; when individuals were put on a diet without carbohydrates and secreted urine containing a great quantity of acetone, the acetonuria disappeared in a few hours when carbohydrates were given. From 150 to 200 grams of carbohydrates per day are required to check an already existing alimentary acetonuria.

In the opinion of Geelmuyden, acetonuria occurs when carbohydrates are not ingested in sufficient amount, and acetone is formed by the disintegration of fat, either of that of the tissues or of that contained in the food. Schwarz and Waldvogel saw also an increase of acetonuria following the fat introduction per os.

PRELIMINARY TESTS FOR ACETONE.—With an alkaline solution of sodium nitrocyanide (of a slightly red hue) acetone gives a ruby-red color, changing, after some time, to yellow, and, after acidifying with acetic acid and boiling, to greenish violet.

The cyanide of soda test, after Le-

gal or le Nobel (see below), may be employed as preliminary test; but, to make the presence of acetone positive, it is necessary to separate it from the urine by distillation. As the boiling point of acetone is low (56.3° C.), this may be done at a low temperature, and the use of a water bath is recommended.

Legal's Test.—To 10 c.c. of urine a small crystal of nitrocyanide of soda or some drops of a freshly made solution of this reagent are added; the fluid is rendered strongly alkaline by a 30 per cent. solution of caustic soda or potash. When acetone is present a beautiful red color will appear, which will change only after some time to yellow; the red color produced in the same manner by creatinin becomes yellow sooner. Legal adds that, when acetone is present and the urine, shortly after the addition of the solution of soda, is neutralized with acetic acid, the urine assumes a purple-red color, and, when diluted with water, a crimson hue. When the acetic acid is floated on the urine a crimson ring will appear at the point of contact, and, when much acetone is present, the color of the ring will be purplish red.

> Legal's test is rendered simpler and more reliable by substituting ammonia for the sodium hydrate. This avoids the disturbing creatin reaction. The urine to be tested is treated with glacial acetic acid and then with a few drops of a freshly prepared solution of sodium nitroprussid; a few cubic centimeters of ammonia are then cautiously poured on top of the mixture. In case of the presence of acetone, a bright-violet ring appears at the point of contact. The violet ring grows brighter and brighter without spreading wider, irrespective of the quantities used in the test-tube or conical glass. The

reaction was most distinct in the writer's tests when 15 c.c. of urine and from 0.5 to 1 c.c. of acetic acid were used. Acetone, 0.025 per cent., is readily detected by this test. Alcohol and aldehyde do not give the reaction. Lange (Münch. med. Woch., Bd. liii, Nu. 36, 1906).

Neither Legal's, Chautard's, nor Lieben's test will detect small quantities of acetone when performed with urine without distillation. After distilling, the iodoform test (Lieben's) is very satisfactory, provided the detection is made by examining microscopically for crystals in form of hexagonal plates or small stars rather than by the odor of iodoform. This test, although reliable, is time-consuming. The writer therefore, prefers Frommer's test, which may be applied to the urine direct. It is as follows: About 10 c.c. of urine are treated with about 1 Gm. of sodium hydroxide in substance, and, without waiting for it to dissolve, 10 or 12 drops of a 10 per cent. solution of salicylaldehyde in absolute alcohol are added. The mixture is heated to 70° C. In the presence of acetone a marked purple-red color develops at the zone of contact with the alkali. This test can indicate the presence of 0.000001 Gm. acetone in 8 c.c. of water.

Unless the urine is diluted so that its specific gravity is reduced to about 1.010, confusing colors occur that render interpretation difficult. When it is properly diluted, however, urine containing only minute or normal quantities of acetone will give, after 10 or 15 minutes' standing, a straw or faintly pink color. Checked against the iodoform test, the Frommer reaction was found very reliable. Muhlberg (Med. Rec., Dec. 27, 1913).

Le Nobel's Test.—Le Nobel and Fehr hold that Legal's test is only reliable when much acetone is present, and that, when there is only a small quantity of it in the urine, the test may be fallacious, since other substances contained in the urine can

produce a red color with the nitro-cyanide of soda. The most characteristic point of the test is, according to Fehr, the appearance of the violet hue, which causes the red color to become crimson or purple, and not pure red.

Le Nobel proposes to substitute a solution of ammonia for the solution of soda, when the test is, in other respects, made according to the indications of Legal; the fluid containing acetone is not immediately colored, but after some time, when the liquid is shaken with air or some drops of a strong acid added (the alkaline reaction being maintained), the fluid takes a rose-red color, increasing gradually and changing after some time to violet wine red. By heating the fluid the color disappears, but returns on cooling down; when boiled with acids it changes into greenish violet. Le Nobel's test is more delicate than Legal's, and will reveal 0.00025 gram of acetone.

Lange thinks the contact reaction gives a more distinct picture than the mass reaction, and modified le Nobel's test in that direction: 15 cm. of urine are mixed in a reagent glass with 0.5 to 1 c.c. of acetic acid and a few drops of solution of sodium nitroprusside. On floating a small amount of ammonia upon this mixture an intense violet ring develops at the point of contact.

Jackson Taylor also modified le Nobel's test. He adds strong ammonia to a fresh-prepared solution of sodium nitroprusside and urine. The ammonia solution remains on the top. There appears—if acetone be present—a well-marked and absolutely characteristic ring of magenta (or petunia) within one to three minutes, and gradually spreads upward, pervading the whole of the ammonia solution if acetone is present in considerable amount.

Fehr's Test.—Fehr also employs the test after the method of Legal, but proposes, when the color of the urine after the addition of solution of soda is passing from dark red to yellow, to float some drops of acetic acid on the urine. When the test-tube is slightly rotated so that only a small quantity of the acid mingles with the urine, a beautiful violet color will appear when acetone is present, the intensity of the color being proportionate to the quantity of acetone contained in the urine.

Chautard's Test.—Romine recommends, as a reliable test for acetone in the urine, a solution of fuchsin (1 : 2000) into which a current of sulphurous acid gas has been passed. This rapidly decolorizes the liquid and causes it to assume a clear yellow tint, which is permanent and unaffected by an excess of acid. A few drops of such a solution, added to a urine containing acetone, produce a deep violet color. The test is delicate enough to allow the detection of 1 part of acetone in 1000 of urine.

DEFINITE TESTS FOR ACETONE.—When no very great quantity of acetone is found in the urine it is absolutely necessary to distill the urine and to test the distillate with the different reagents. The distillation of 200 to 300 c.c. of urine (always fresh, since acetone can disappear when the urine has to stand hours in a warm place) is made in a water bath, and a temperature of 56° to 58° C. employed. No acid need be added to the urine before

distillation, as the acetone becomes distilled very well without acid and the acid might disintegrate other substances present and thus cause the formation of acetone. There is no reason why special care should be taken lest a small amount of ammonia be distilled with the acetone. The distillation is only continued until a sufficient quantity of fluid for the different tests to be employed has passed over into the recipient. The distillation is then subjected to the following tests:—

Lieben's Iodoform Test.—To a few c.c. of the distillate a few drops of a solution of potassium and some drops of a solution of iodine and iodide of potassium are added, the solution of potassium being added in excess. When acetone is present, a thick, yellow precipitate of iodoform will immediately form. This test will reveal 0.01 mg. By heating, the iodoform evaporates and accumulates on the sides of the test-tube in the form of small yellow plaques, consisting of the characteristic crystals (hexagonal plaques and stars) of iodoform. The most serious objection to Lieben's test is that many (at least seventeen) other substances, and especially alcohol, may give the same result.

Gunning's Test.—Gunning modified Lieben's test by using a solution of ammonia and tincture of iodine. Le Nobel prefers to use a solution of ammonia and iodine dissolved in iodide of ammonium; this certainly is the best way to make the iodoform test, as no alcohol is added with the reagents. According to le Nobel, 0.001 mg. of acetone can be detected by this test, but von Jaksch could only detect acetone by it when present in a quantity of 0.1 mg. Errors caused by the presence of alcohol and aldehyde are avoided by this test.

Reynold's Test.—Freshly precipitated oxide of mercury is dissolved by acetone in the presence of alkali. Le Nobel prefers to make the test by precipitating a solution of perchloride of mercury with an alcoholic solution of caustic potash, added until the mixture gives a strong alkaline reaction; then the fluid containing acetone is added and the whole well shaken in a test-tube. The fluid is then filtered and care taken that the filtrate be perfectly limpid. The combination of acetone and oxide of mercury in the filtrate can be detected by chlorate of stannum or by floating some drops of the filtrate on a solution of sulphide of ammonium: where the two liquids touch each other a black ring will appear. By means of this test 0.01 mg. of acetone is revealed, but aldehyde is also able to dissolve a rather considerable quantity of mercuric oxide.

The Nitrocyanide Test.—This test is made with the distillate quite in the same manner as with the urine, either after the method of Legal or after le Nobel's modification of it. This test is less delicate, and the phenols, which possibly might have passed over into the distillate, are apt to give the same color as the acetone; the test, therefore, gives no proof of the presence of the latter substance.

Penzoldt's Indigo Test.—Baeyer and Drewsen found that acetone forms indigo blue with orthonitrobenzaldehyde. Penzoldt has employed this reagent by dissolving crystals of orthonitrobenzaldehyde in boiling water; on cooling down the aldehyde forms a white, milky cloud; the fluid

which is to be tested is now added and the mixture rendered alkaline with a solution of sodium hydrate. When acetone is present a yellow color will appear, which changes to green and, after ten minutes, to indigo; it also forms an indigo-blue precipitate. Very small quantities of acetone may be detected by shaking the mixture with a few drops of chloroform. When left quiet for some time the chloroform takes a blue color and sinks to the bottom of the test-tube.

According to Penzoldt, acetone is revealed by this test in a solution of 1 to 2000. According to von Jaksch, the smallest quantity of acetone revealed by it is 1.6 mg. Aldehyde acetophenone and other substances form indigo in the same way as acetone, but the color is not so marked.

Malerba's Test.—Malerba found that a ½ per cent. solution of paramidomethylaniline with acetone gives a reddish color, changing into violet and blue-red.

Riegler describes the following test: 15 cm. of urine are acidulated with 5 to 10 drops of concentrated sulphuric acid. When 2 to 3 c.c. of an aqueous solution of iodic acid are added, an intense pink color will appear, which is not taken up by chloroform. The test has been found to be specific and active where Legal's test fails.

Frommer renders the urine strongly alkaline with potassium hydrate and adds several drops of a 10 per cent. solution of salicylic aldehyde, and heats to 70° C. A purple ring appears if the reaction is positive.

Miscellaneous Tests.—With bisulphite of soda, acetone, as well as the aldehydes, combines to a crystallic compound in thin flakes resembling those of cholesterin, even by microscopic examination (Limpricht).

Acetone in an alkaline solution combines with iodine to form iodoform.

Freshly precipitated oxide of mercury is dissolved by acetone. Indigo is formed when acetone is combined with orthonitrobenzaldehyde in an alkaline solution. (Baeyer and Drewsen.)

From what has just been stated it will become apparent that not one of the tests is specific for acetone alone. To be quite sure that acetone is contained in the distillate, it is necessary to try successively by all the tests, and only when all tests give positive result is the presence of acetone proved.

A. E. Taylor is of the opinion that only the tests described by Stock and Denigés are really good and reliable and should replace the tests with Lugol's solution, mercuric oxide and sodium nitroprusside.

The only two really good tests for acetone in the urine are that of Stock, described in 1899, and that of Denigés, described in 1898. These are certain in their results and easy of execution, and should replace the fallacious tests with Lugol's solution, mercuric oxide and sodium nitroprusside. The two tests agree; the writer has never had the Stock test present without the Denigés test being also positive. The Stock test is less sensitive than the other, but this is considered an advantage for practical purposes. The author has often found acetone present by these tests without obtaining the reaction for diacetic acid, for which he also gives the method; but he has never found diacetic acid present without acetone. A. E. Taylor (Jour. Amer. Med. Assoc., Mar. 17, 1909).

he quantitative estimation of the acetone bodies is often most important as an indicator of the degree of

derangement of metabolism and acidosis that may be present.

Von Jaksch has tried to employ the nitrocyanide test for a quantitative estimation of the acetone, and the iodoform test has been recommended by Messinger and Huppert for the same purpose. The quantity of iodine used to form iodoform with the acetone is measured (titrated), and the quantity of the acetone present in the solution calculated by it also; but, although Engel and Devoto are of the opinion that it is possible to make pretty accurate estimations in this way, methods for quantitative estimation of the actone are not to be relied upon, as it is impossible to avoid errors caused by the presence of substances which are influenced by the tests in the same way as the acetone.

Diacetic acid ($C_4H_6O_3=CH_3$—CO —CH_2—COOH) may be revealed in the urine by the aid of a solution of perchloride of iron (Gerhardt's test), which, with diacetic acid, produces a dark wine-red color. The test is made by adding a solution of perchloride of iron as long as a precipitate of phosphates of iron is formed. The mixture is then filtered and some drops of perchloride are added to the filtrate. When diacetic acid is present, the filtrate takes a deep-red color, which vanishes in twenty-four hours, and more rapidly after addition of strong acids. Von Jaksch has, by a colorimetric method based on this test, tried to make an approximate estimation of the quantity of diacetic acid contained in the urine, but newly passed urine can alone be used for the search of diacetic acid, as this acid, after some time—twenty-four to forty-eight hours—will disappear from the urine. Diacetic acid can be isolated from the urine by adding a few drops of sulphuric acid and shaking the mixture with ether. When diacetic acid is present, it is dissolved in the ether and can be detected by the perchloride of iron test.

Beta-oxybutyric acid ($C_4H_8O_3$) is also found sometimes in the urine of fever patients, as well as in diabetes, with acetone and diacetic acid. This may also be the case in the dyspepsia of alcoholism and in carcinoma of the stomach, scarlatina, measles and scorbutus. When beta-oxybutyric acid is cautiously oxidized, acetone is found.

For general practice the exact quantitative determination of the acetone bodies is rather complicated. To overcome this difficulty, Stuart Hart (1908) devised a procedure based on the delicacy of the well-known test-tube reactions in urine. The urine is first tested for Gerhardt's reaction. If positive, we know the acetone bodies to be present in excess of 0.2 Gm. per liter. If the reaction is very strong, the test solution is diluted with distilled water until the color approximates that of the standard ferric chloride solution, and this dilution, when compared in one of the author's tables, gives the amount in Gm. per liter.

If Gerhardt's reaction proves negative, Arnold's, Legal's and Lieben's tests are tried in the order named. A positive Arnold reaction indicates Ca 0.1 Gm. per liter; positive Legal reaction Ca 0.03 Gm. per liter. If only Lieben's test is positive, the amount of acetone is within the normal limits. (See ACIDOSIS, this volume.)

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ACETOZONE, a germicide and deodorant (accepted by the A. M. A. Council) formerly known as *benzozone,* is a mixture of acetylbenzoyl peroxide and an inert absorbent powder. It was introduced by Freer and Novy, of the University of Michigan. Its properties resemble those of hydrogen peroxide, though, according to its discoverers, it is over one hundred times more active as a germicide.

Acetozone, in its original form, occurs as white shining crystals, but is marketed in the form of a powder. The latter should be kept perfectly dry, but it should not be exposed to heat, which decomposes and volatilizes it. It is also rapidly decomposed by organic substances and should not be administered after a meal.

Modes of Administration.—Acetozone is usually employed in the following manner: "Add the powder to warm water in the proportion of 15 grains to the quart; shake vigorously for five minutes, and allow to stand for about two hours. Decant off the liquid as required. If the patient objects to the taste, a little extract of orange or lemon, or orange or lemon juice, ginger ale, carbonated water, or fruit syrup may be added to each dose as taken." It may also be given in capsules, but followed at once by a copious draught of water.

It is soluble in water to the extent of 1 : 1000 to 10,000; in its crystalline form in oils to the extent of about 3 per cent. and slightly soluble in alcohol, ether, and chloroform, but all these solvents gradually decompose it. This does not apply to neutral petroleum oils, however, and an *"acetozone inhalant"* is available which contains 1 part of acetozone, ½ part of chloretone, and 98.5 parts of refined liquid petroleum. It may be given in an *ointment,* using solid or liquid petrolatum as excipient, beginning with ½ per cent. strength. An aqueous solution may be used as *spray* and as a *deodorizer* and *antiseptic* for stools, sputum, etc.

Therapeutics.—Acetozone is used for its marked oxidizing and germicidal action mainly for the treatment of diseased mucous membranes. It has been credited with a favorable action in **typhoid fever,** the main effect being decrease of the fetor of the stools, subsidence of the tympanites and diarrhea, and prevention of hyper-pyrexia. Good results have been obtained in **Asiatic cholera.** In ophthalmology, a solution of 1 grain to 2 ounces of water, instilling 1 drop or 2 every hour, has been found useful in **corneal infections.** In laryngology, **tonsillitis** and **atrophic rhinitis** have seemed to be beneficially influenced. This applies also to **infected wounds, gonorrhea,** and **chancroid.** It has been found an excellent deodorant in **gangrene** and malignant **small-pox.**

Acetozone is a very efficient bactericide and antiseptic for use in the treatment of **war wounds.** It may be used in strengths of from 5 to 10 grains (0.3 to 0.6 Gm.) to the pint (500 c.c.) for wet dressings and irrigations and to saturate gauze. It can also be used in the stronger solutions by Carrel's method. In very septic cases the strengths may be raised to 20 or even 60 grains (1.3 to 4.0 Gm.) to the pint (500 c.c.). The solution keeps fairly well, but should be made fresh every week. Bacteriological tests showed that it was markedly germicidal toward Staphylococcus pyogenes as well as the anærobic Bacillus mycoides, which is a spore bearer. Its germicidal power is considerably reduced, however, in the presence of serum, broth, or pus, but it still remains fairly efficient. C. Gore-Gillon and R. T. Hewlett (Brit. Med. Jour., Aug. 18, 1917).   S.

ACETPARAMIDOSALOL.

See SALOPHEN.

ACETPHENETIDIN.—

(*acetphenetidinum;* para-acetphenetidin), commonly known under the proprietary name of *phenacetin,* is a coaltar product, obtained by treating para-phenetidin with glacial acetic acid. It is an acetyl derivative [C_6H_4. OC_2H_5. $NH\,CH_3CO$] of para-amidophenol.

PROPERTIES.—Acetphenetidin occurs in the form of a white, odorless, and practically tasteless powder, composed of small, needle-like or scaly crystals.

DOSE.—Five to 10 grains (0.32 to 0.65 gram) in adults; 1 to 5 grains (0.065 to 0.32 gram), according to age, in children. The *maximum* amount to be given in twenty-four hours, according to Pouchet, is 30 to 45 grains (2.0 to 3.0 grams), which should be distributed during the day in several doses, each not exceeding 7½ grains (0.5 gram). The tendency is toward a marked decrease of this amount.

> Out of 297 observers using acetphenetidin, 10, or 33 per cent., employed less than 2 grains as a minimum dose for adults; 90, or 30.3 per cent., employed 2.5 grains or less as a minimum dose; 188, or 63.3 per cent., employed from 3 to 5 grains as a minimum dose; 89, or 29.9 per cent., used doses exceeding 5 grains, while 208, or 70 per cent., never exceeded a dose of 5 grains.
>
> An examination of a number of prescriptions for adults on file in various pharmacies in Washington, D. C., showed that the average dose of acetphenetidin prescribed was 1.92 grains. Kebler, Morgan, and Rupp (U. S. Dept. of Agricul., Bureau of Chemistry, Bull. No. 126, July 3, 1909).

MODES OF ADMINISTRATION.—Acetphenetidin is almost insoluble in cold water (1 grain in 2 ounces), more freely soluble in boiling water (1 grain in 1 dram), and readily so in alcohol (1 grain in 12 minims); it will also dissolve in glycerin and lactic acid.

Being almost tasteless, it is easily taken in powder form; it can also be given in capsules, cachets, or tablets. When combined with other remedies in liquid preparations it is best kept in solution by dilute alcohol. Thus a mixture of acetphenetidin, sodium bromide, and caffeine in the elixir of licorice is frequently prescribed for the relief of headache. A good formula is the following:—

R *Acetphenetidini* ..... gr. xv (1.0 Gm.).
   Caffeinæ citratæ ..... gr. viij (0.5 Gm.).
   Sodii bromidi .... ʒj (4.0 Gm.).
   Elixiris glycyrrhizæ. ʒj (30.0 c.c.).

M. Sig.: Two teaspoonfuls, repeated if necessary. Shake well.

Where nausea and vomiting accompany headache, oral administration being, therefore, unsuitable, acetphenetidin may be administered by the rectum in 1 or 2 drams of water (Brunton).

Acetphenetidin is sometimes used locally in powder form or in an ointment or alcoholic preparation.

INCOMPATIBILITIES.—Acetphenetidin is incompatible with iodine, nitric acid, and oxidizing agents generally; also with chloral hydrate, phenol, and salicylic acid.

CONTRAINDICATIONS.—These are the same as those of acetanilide (*q.v.*), though the dangers from its use are less marked than with the latter drug. It is advisable not to employ it in cases of heart disease, pulmonary tuberculosis, grave anemia, or in persons markedly enfeebled from any other cause.

PHYSIOLOGICAL ACTION.— **As Antipyretic.**—Acetphenetidin is the safest and most frequently employed of antipyretic remedies. In common with acetanilid, it has little or no influence on the temperature of normal individuals in therapeutic doses, but causes a fall in febrile cases. According to Crombie and Hirschfelder, the greatest reduction is not produced until three or four hours after administration. The average decline may be put down as 3.6° F. (2° C.; Manquat). The reduction may last six to eight hours, and is free of unpleasant effects, excepting a mild sweat (Pesce). Cerna and Carter found that acetphenetidin produced a very slight fall of temperature during the first and second hours after inges-

tion, and that the effect reaches its height in the third hour. They believe that the fall of temperature results chiefly from a decrease in heat production, together with a slight increase in the heat dissipation, less marked than in the case of antipyrin. Probably the delayed action of the drug depends on its insolubility. It should be mentioned, however, that certain authors describe its effect as being more prompt, and comparable with that of acetanilide.

With regard to the manner in which the antipyretic effect is produced, the prevailing belief is that it depresses the heat-regulating centers.

As Analgesic.—Acetphenetidin is considered to exert a sedative effect upon the nervous system. Its anodyne influence is more marked than that of acetanilide or antipyrin. It is believed to depress the nerve-centers, in common with the other antipyretics, but it has probably also some action on the sensory nerves, since it frequently relieves neuralgic pain without giving evidence of any central depressant action by the production of drowsiness or mental apathy.

Injected into animals, large doses of acetphenetidin are required before its effects on the nervous system appear. Using doses of 0.5 to 1 Gm. per kilo of body weight in rabbits, Mahnert observed merely a muscular weakness, lasting a few hours, which he ascribed to a depressing action on the spinal cord. With doses of 3 Gm. per kilo he obtained a short period of spinal excitation, followed by one of complete motor and sensory paralysis, with loss of reflexes and early death. In frogs the preliminary spinal excitation may be such as to produce convulsions. In mammals convulsions produced by the antipyretics may be of cerebral, spinal,

or, possibly, asphyxial origin (Cushny). H. C. Wood, Jr., and H. B. Wood watched the effects of acetphenetidin on frogs when absorbed through the skin from a saturated solution. Like Mahnert, they noted a sluggishness of movement and loss of muscular power, proceeding steadily to complete paralysis, with final cessation of the heart beats. In addition, they found that the motor nerves and the muscles, though soaked in saturated acetphenetidin solution, continued responsive to electric stimulation throughout the period of action of the drug, and even after death, and concluded, therefore, that the loss of reflexes and paralysis observed had been of spinal origin. They ascertained that doses of 0.5 Gm. per kilo, injected into the jugular vein of a dog, caused death from paralysis of respiration.

Local applications of acetphenetidin have some analgesic effect.

On the Circulation.—Conflicting views have been advanced by different observers concerning the effects of the drug on the blood-pressure. Cerna and Carter found that, in moderate doses, it caused a rise of the arterial pressure by directly stimulating the heart's action, and also, probably, the vasomotor system, while in large doses it decreased the pressure, chiefly by its influence on the heart. They also state that acetphenetidin tends to increase the pulse rate, mainly by cardiac stimulation, and possibly, also, by influencing the cardio-accelerator apparatus, while later, especially with large doses, it decreases it primarily by stimulating the cardio-inhibitory centers, and later by depressing the heart. Ott and H. C. Wood, Jr., on the contrary, assert from their experiments that acetphenetidin does not influence the blood-pressure. Mahnert considers the drug to be antago-

nistic to strychnine in its physiological action, large doses producing paralysis of the cardiac and respiratory centers. In the early stage of its action, however, it is believed to stimulate these centers for a time.

On the Blood.—Alterations in the blood are much more rarely caused by acetphenetidin in moderate doses than by acetanilide. The formation of met-hemoglobin has, however, been observed in a few cases. According to Cushny, this untoward result is due to the action of para-amidophenol, into which the drug is gradually decomposed in the organism. Cerna and Carter were unable to produce methemoglobinemia in their experiments on animals.

Acetphenetidin is said to have a slightly stimulating influence on the sweat-glands, which is not possessed by the other antipyretics.

Elimination.—Acetphenetidin is believed to be eliminated chiefly in an altered condition, losing its acetyl radicle in transit through the organism, and appearing in the urine as glycuronates of phenetidin (Cushny). The gastric and pancreatic juices being without influence on the drug *in vitro,* F. Müller believes that the decomposition must occur after it has been absorbed. According to Gueorguievsky, the elimination by the urine begins in twenty minutes and proceeds rapidly. Perchloride of iron added to this urine causes a Burgundy red color to appear. Acetphenetidin may also be eliminated in part by the skin, since Hirschmann not infrequently found large numbers of crystals precisely similar to those of the drug on the skin of persons to whom it had been administered.

UNTOWARD EFFECTS AND POISONING.—H. C. Wood states that no symptoms are produced by the therapeutic dose of this drug. Even large doses of it have been given so often without markedly unpleasant results that, in contrast with acetanilide and antipyrin, it has frequently been described as non-toxic. Massive doses, however, and even moderate doses in certain susceptible individuals, have been known to cause untoward effects similar to those of the other coal-tar antipyretics. The most commonly observed of these have been profuse sweating, somnolence, lassitude, sometimes accompanied by nausea, vertigo, or chilliness. In more severe cases there have occurred cyanosis, beginning and most marked in the face, lips, and finger-tips, then becoming general; prostration, vomiting, palpitation, dyspnea, anxious expression, followed by collapse, which occasionally is fatal. The blood may be darkened by the formation of methemoglobin. The urine has been found to contain blood (Krönig). In a case reported by Hollopeter three doses, of 7 grains each, of phenacetin sufficed to produce in a woman severe precordial pains, great dyspnea, general lividity, somewhat dilated pupils, and collapse, with unconsciousness; recovery took place after a week. Cutaneous eruptions, usually urticarial, are sometimes caused, though less frequently than by antipyrin. As with acetanilide, the onset of the symptoms is frequently sudden and unexpected, the patient having previously borne repeated doses without harmful effect.

A girl of 16½ years, in good general health, but having a headache and feeling that she had taken cold, took 2 headache tablets and went to bed. About an hour and a half later her lips and face began to grow blue, and a physician was sent for. Responding at once, he found the girl with pronounced cardiac weakness

and edema of the lungs. Before any remedy could be administered she died. The tablets she had taken, labeled "Danbury's headache tablets," were subsequently found on examination to contain acetphenetidin. G. L. Tobey (Mo. Bull., State Board of Health of Mass., Jan., 1908).

Of 70 cases reported by 41 observers in the literature from 1887 to 1907, 3, or 4.2 per cent., terminated fatally. Sixty-three of the 70 cases were reported during the years 1887-90, *i.e.*, in the period just following the advent of acetphenetidin as a medicinal agent, when the drug was used freely in asthenic as well as sthenic affections. The most prominent ill effect was general systemic depression, which was present in 38.5 per cent. of the cases. In 17.1 per cent., it amounted to actual collapse. Cyanosis was reported in 34.3 per cent. of the cases, skin affections of various kinds in 30 per cent., dyspnea in 14.3 per cent., and disturbances of the renal function in 10 per cent. Kebler, Morgan, and Rupp (U. S. Dept. of Agricul., Bureau of Chemistry, Bull. No. 126, July 3, 1909).

Treatment of Acute Poisoning.—No special reference to this subject having been found in the literature, we can only recall the plan of treatment used for poisoning by the other coal-tar derivatives, the toxic effects of which are identical. Stimulants to the circulation and respiration, such as **strychnine, atropine, aromatic spirits of ammonia, ether** hypodermically, and **digitalis; saline solution** by enteroclysis or hypodermoclysis, etc. The application of **heat** to the body should never be neglected in cases of collapse. **Artificial respiration** is always valuable, and inhalations of **oxygen** may be resorted to as an ultimate measure.

CHRONIC POISONING.—While not as frequent as chronic acetanilide poisoning, chronic acetphenetidin poisoning is nonetheless fairly common.

The symptoms show a great similarity to those produced by the habitual use of acetanilide, consisting chiefly of nervous and digestive disturbances, a cyanotic coloration of the skin, anemia, and weakened heart action.

Instances of chronic poisoning have been reported by several clinicians. J. S. Davis observed a case in a woman, previously "a healthy, buxom country girl," who had been addicted to the acetphenetidin habit for about seven months, ingesting from 15 to 20 grains daily. The habit was found out by her husband when her supply of the drug gave out and the local pharmacist also ran out of a supply temporarily. Violent convulsive and hysterical seizures appeared, and continued until acetphenetidin had been obtained for her. The pulse rose to 170 and became feeble; respiration, 30, spasmodic; pupils widely dilated; pallor and cold perspiration. The patient had over a dozen convulsions and vomited freely. Examination subsequent to the attack showed some anemia, poor complexion, weak circulation, pulse 124, sleep restless and troubled, digestion impaired, occasional vertigo.

From collective reports of cases it would appear that toxic manifestations are somewhat less likely to develop when acetphenetidin is taken habitually than when acetanilide is the drug used.

In the replies of 400 physicians to a set of questions sent out by the Bureau of Chemistry of the U. S. Department of Agriculture, 112 instances of the acetanilide habit were reported, 7 of the antipyrin habit, and 17 of the acetphenetidin habit. The number of cases in which ill effects were observed from the use acetanilide was 85, from antipyrin 2, and from acetphenetidin 7. The chief symptoms observed from the habitual use of these drugs were: Nervous depression, 44 cases; cyanosis, 27; cardiac depression, 18; anemia, 15; dyspnea on exertion, 8; insomnia, 4; constipation, 3; edema, 2;

increased headache, 2; icterus, 1; muscular twitchings, 1; loss of sexual power, 1. In 5 of the cases of acetphenetidin habit protracted ill effects were noted, as compared with 32 instances in case of acetanilide and 2 instances in case of antipyrin. The chronic symptoms oftenest noted were anemia, general debility, nervousness, and weak and irregular heart action. Kebler, Morgan, and Rupp (U. S. Dept. of Agricul., Bureau of Chemistry, Bull. No. 126, July 3, 1909).

Treatment of Chronic Poisoning.— The measures required upon withdrawal of the drug will generally comprise the use of **stimulants, saline laxatives,** and **codeine.**—the latter used with caution in amounts just sufficient to mitigate pain and favor sleep (*v.* Treatment of Chronic Acetanilide Poisoning).

THERAPEUTICS.—As Antipyretic.—Acetphenetidin is generally considered the safest of the coal-tar antipyretics. Its effect in reducing temperature is marked; as previously stated, its action begins in about thirty minutes and reaches its maximum in three to four hours. According to Heusner, 1 Gm. (15 grains) of this drug is the equal in antithermic power of 0.5 Gm. (7½ grains) of acetanilide, and 2 Gm. (30 grains) of antipyrin. The relative infrequency with which it causes cyanosis, depression, and other unpleasant or dangerous effects recommends its general use as an antipyretic in preference to the older coal-tar remedies if used at all. The employment of antipyretics other than hydrotherapy and other external measures is decidedly on the wane, however, in the hands of competent clinicians.

Exception to this is probably only to be made where prompt reduction of fever is required, as in cases of hyperpyrexia; here acetanilide, whether used in conjunction with hydrotherapeutic measures or not, may prove more effective than acetphenetidin. It is believed, however, that the effect of the latter drug is more lasting than that of acetanilide; the greater tendency of which to depress the circulatory and respiratory organs should also be remembered. As stated above, however, the use of antipyretics in the various forms of fever is now deemed inadvisable by most authorities. Moreover, these agents, by causing the temperature records to lose their characteristic features, may impair their value for diagnostic and prognostic purposes. The alleged prejudicial influence, on the other hand, that chemical antipyretics have been said to exert on the substances of the blood-serum that antagonize disease has been shown not to exist, at least in the case of the agglutinating bodies of typhoid serum (Sollmann). When delirium is present in fever, the mild narcotic action exerted by the coal-tar antipyretics, especially acetphenetidin, may prove useful.

As an Analgesic.—Phenacetin is chiefly of value for the relief of pain, especially of pain of the neuralgic type. In pains due to gross inflammations or deep-seated distress, the result of organic disease of viscera, morphine is far more effective than phenacetin. But in pains due to nervous disorders, especially **neuralgia** and **neuritis,** and in various forms of **headache,** acetphenetidin has come to be considered almost as a specific. In **hemicrania,** in **headache due to eye-strain or insufficiency** of certain of the extraocular muscles, in **intercostal neuralgia, sciatica, gastralgia,** and in the pains of **tabes dorsalis,** acetphenetidin frequently affords considerable relief.

The manner in which this drug, in common with other coal-tar antipyretics, acts in relieving headache has not yet been definitely ascertained. According to Brunton, headache is associated with and caused by what he terms a "colic" of the arteries of the head, the peripheral vessels being contracted and the central vessels dilated; the drug would presumably give relief by overcoming this abnormal condition of the cephalic arteries. E. Weber has recently demonstrated experimentally in dogs whose brain had been exposed that coal-tar drugs cause constriction of the vessels on the surface of the cerebrum.

It is well known, moreover, that caffeine, an undoubted vasoconstrictor, when combined with the coal-tar drugs, greatly assists their analgesic action in headaches. Hence it would seem as if the relief given in these cases were due, in some way, to a modification in the caliber of the vessels.

In **acute rheumatism**, acetphenetidin has been found useful as an analgesic in doses of 3 to 8 grains (0.2 to 0.5 gram), given every four hours. A valuable combination is 4 grains each of acetphenetidin and salol, given three or four times daily. Eldredge counsels the administration of acetphenetidin in powder and salicylic acid in solution, the dose of each being regulated according to the patient's susceptibility and the severity of the attack. In cases with cardiac complications, he claims not to have observed any depressing action on the heart when the drug was given to reduce fever. Hirschfelder noted specially the fact that sometimes a hypnotic action seemed to be produced. In **subacute rheumatism** and in **lumbago** and other **rheumatic muscular pains,** the drug is also frequently effective.

In **gonorrheal rheumatism,** acetphenetidin was found by Eldredge to act well when given with potassium iodide and sodium salicylate.

In **influenza,** acetphenetidin has become a favorite remedy. The pains in the head, back, and limbs are relieved, and the fever reduced. The drug may be given alone in powder form, or combined with other remedies, *e.g.*, quinine. In this disease, essentially an asthenic disorder, it is important that the analgesia be secured with the least possible degree of general depression; hence acetphenetidin should always be given the preference over its more depressing congeners—acetanilide and antipyrin.

Acetphenetidin and other coal tar preparations have been successfully employed in the treatment of **migraine** and in **neuralgia.** Pharmacologists assume that these results are obtained by a chemical blocking of the nerves that mediate sensations of pain, said blocking taking place presumably in the region of the thalamus. So efficient have these products proved in wisely selected cases, that their use seems at present to be justifiable, despite their undeniable ulterior effects, many of which are sometimes exceedingly alarming and some of which have resulted in fatalities. In using these preparations it should be strictly borne in mind that the obvious benefits secured in neuralgia and migraine are palliative only; the drugs are in no sense curative, even though their power to give grateful alleviation may readily continue until the provocative cause of the distress has more or less completely disappeared. The aim should be to ascertain the source of the neuralgic toxin and eliminate it.

One should select the less poisonous of the several products, acetphenetidin for example, and administer it in the smallest adequate doses, 0.2 to 0.6 Gm. (3 to 10 grains) being usually sufficient. A. D. Bush (N. Y. Med. Jour., Jan. 15, 1916).

In **whooping-cough,** acetphenetidin diminishes the severity and frequency of the paroxysms. In children, 1 or 2 grains (0.06 to 0.013 gram), given three or four times daily, are generally sufficient.

Chorea has also been treated with acetphenetidin. Like the other coal-tar drugs, acetphenetidin exerts a not inconsiderable effect on the motor functions and reflex action, as well as on general sensibility. Hence the fact that it sometimes proves useful in this disorder.

Insomnia, the result of overwork or general nervous excitability, may yield to acetphenetidin. Kiernan reported having seen it bring on sleep in persons suffering from insomnia due to simple exhaustion. In view of the possible serious depressive effects from an overdose, the likelihood of a drug habit being formed, and the fact that much safer and better hypnotics are available, it seems doubtful whether the use of acetphenetidin for this purpose should be encouraged.

The same is probably true of the use of acetphenetidin in the initial stage of **pneumonia,** in which it has been employed to relieve distress, bring on sweating, reduce fever, and favor sleep. If the drug is used at all, it must surely be withdrawn as soon as the patient begins to show pronounced general depression and signs of lowered circulatory activity. In pleurisy acetphenetidin has likewise been used to relieve the pain of the initial stage.

The first stage of **acute coryza** may be shortened by giving a few doses of acetphenetidin, which will not only promote sweating and lower the temperature, but also relieve the unpleasant accompanying sensations. A powder containing 5 grains (0.3 gram) each of acetphenetidin and salol, together with 1 grain (0.06 gram) of citrated caffeine, may be administered every three hours for 3 doses with advantage.

In **diabetes mellitus** acetphenetidin, in common with other coal-tar drugs, has been prescribed, generally with but temporary benefit.

Local Uses.—Acetphenetidin is sometimes used externally for its analgesic and antiseptic properties. Dusted in finely powdered form on the raw surfaces of **ulcerations** of various kinds, it not only relieves pain, but favors the development of healthy granulations, thereby hastening the healing process. Because of its low degree of solubility in water, as compared with antipyrin and acetanilide, the likelihood of the absorption of a toxic amount of acetphenetidin from open surfaces is somewhat less than with the above-mentioned agents. Nevertheless, this danger should always be kept in mind, and the external use of the drug confined to lesions covering a small area only.

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ACETYLENE.—When calcium carbide (CaC_2) is brought in contact with water, acetylene gas is formed. Being capable, when ignited, of furnishing a degree of light far superior to that of ordinary gas, acetylene has in recent years been considerably used as an illuminant. When prepared from pure calcium carbide and purified by liquefaction, it has a pleasant ethereal odor and can be breathed in small quantities without giving rise to ill effects. Impure gas, prepared from coal or impure lime, may contain calcium sulphide and phosphide, and the acetylene prepared from it may then have a very unpleasant odor.

Acetylene Poisoning.—Acetylene may be fatally poisonous when present in propor-

tions as high as 40 per cent. by volume, as shown by Gréhant, Berthelot, and Moissant. A mixture of 20 volumes of acetylene—prepared from calcium carbide, 20.8 volumes of oxygen, and 59.2 volumes of nitrogen—was breathed by a dog for thirty-five minutes without any marked disturbance, and 100 c.c. of the blood were found to contain 10 c.c. of acetylene. With 40 volumes of acetylene, the proportion of oxygen remaining the same, a dog died in less than an hour, owing to failure of the heart's action, and 100 c.c. of blood contained 20 c.c. of acetylene. With 79 volumes of acetylene and 21 volumes of oxygen the poisonous effects were still more strongly marked.

The poisonous action of acetylene itself is feeble when the blood is at the same time supplied from the air with the usual amount of oxygen. In other words, acetylene inhaled in the open air is but slightly harmful. Brociner found that 100 volumes of blood dissolve about 80 volumes of acetylene; the solution shows no characteristic spectrum, and is reduced by ammonium sulphide as readily as ordinary arterial blood. If any compound of acetylene and hemoglobin is formed, it is very unstable, and is not analogous to carboxyhemoglobin.

In a closed room, however, where the oxygen is not kept up to the normal standard, when the accumulation of a foreign gas would prevent the constant renewal of air through window and door interstices or open chimneys, and where the products of respiration would be allowed to accumulate, it would quickly prove mortal by paralyzing the respiratory function. Mosso and Ottolenghi found experimentally that acetylene has considerable toxic power. One pint of the pure gas caused severe symptoms of poisoning in dogs, and even when mixed with air (20 per cent.) it proved fatal after an hour. If the gas was administered rapidly, the animal recovered when placed in the open air, but if given slowly this did not occur, and the animals died.

Thomas Oliver has shown that a mixture of air and acetylene commences to be explosive when it contains 5 per cent. of acetylene, whereas it requires the presence of 8 per cent. of coal gas to make a similar mixture explosable. If a rabbit is placed in a bell-jar into which ordinary air and acetylene are pumped, the animal seems for a long period to experience very little inconvenience. It is not until ordinary atmospheric air is excluded and only acetylene admitted that symptoms gradually and slowly develop. After a more lengthened exposure to acetylene than that which is necessary for coal gas the animal becomes intoxicated, it falls over on its side apparently profoundly asleep, and, while all through the experiment its breathing has been somewhat short and rapid, stupor steals over the animal apparently painlessly. A few inhalations of atmospheric air are sufficient to restore to the animal all its faculties. Should inhalation have been pushed further and the animal have been very deeply asphyxiated, death may ensue, cyanosis, hitherto observed, being rapidly replaced by extreme pallor.

Treatment of Acetylene Poisoning.—That **fresh air** should at once be given the patient need hardly be mentioned. The patient should be removed from the poisoned atmosphere into a well-ventilated room and **artificial respiration** practised. Hypodermic injections of **strychnine** and **digitalis** should be administered while **oxygen** is sent for. This gas should be inhaled as soon as practicable, while artificial respiration is continued with vigor, the patient being simultaneously rubbed. **Rectal injections of warm coffee** are also useful. **Hypodermoclysis**, with **epinephrin or adrenalin** 1 : 1000 solution introduced drop by drop into the **saline solution** by pushing the hypodermic needle into the rubber pipe, is indicated in all cases of severe poisoning by the gas.

In all such cases the efforts of the physician should be kept up a long time, the respiration and pulse being unreliable guides as regards the presence in the system of sufficient life to render resuscitation possible.   S.

ACIDITY OF THE GASTRIC CONTENTS, TESTS FOR.—While the acidity of normal gastric juice is due mainly to the presence of hydrochloric acid, departures from the normal proportion of this acid in the gastric contents have been

found to accompany with sufficient frequency certain disorders to facilitate the recognition of these disorders. Thus, a proportion of hydrochloric acid of 0.15 to 0.3 per cent. represents the acidity found under normal conditions, *i.e.*, *euchlorhydria*, but an excess of acid, *hyperchlorhydria*, is common in gastric ulcer, gastroptosis, hysteria, tabes, and other disorders. *Hypochlorhydria*, a deficiency of hydrochloric acid, also accompanies various disorders, especially gastric cancer, neurasthenia, anemia, chronic gastritis of long duration, gastric neuroses, and certain diseases of the pancreas, while *achlorhydria*, absence of hydrochloric acid, is found in advanced cases of the same disorders. Again, the fact that hydrochloric acid is necessary to peptic digestion, while acting as a powerful antiseptic to the ingested foodstuffs, further indicates the practical importance of ascertaining accurately the acidity of the gastric contents.

To obtain accurate information, it is necessary to administer a test-meal containing a definite quantity of foodstuffs, and to leave the latter in the stomach a definite time.

Test-meals.—Those described are generally given preference:—

The *Ewald-Boas breakfast* consists of 1 roll weighing about 35 Gm. (9 drams) and a large wineglass of 300 Gm. (10 ounces) of water. This meal should be taken early in the morning on an empty stomach, the bread being eaten slowly and the water sipped while this is done. At the end of one hour, 20 to 60 c.c. (5 to 10 drams) of the meal should be withdrawn from the stomach in the manner indicated below.

The *Leube-Riegel test-meal* consists of beef soup, 400 c.c. (12 ounces); beefsteak finely chopped, 200 Gm. (6 ounces); wheat bread or potato, 50 Gm. (1.6 ounces), and water, 200 Gm. (6 ounces). The gastric contents should be removed at the end of four hours.

The *Salzer method* includes two meals: The first consists of 30 Gm. (1 ounce) of lean roast beef chopped very fine; milk, 250 c.c. (8 ounces); rice, 50 Gm., and 1 soft-boiled egg. The second meal, given four hours later, is an Ewald-Boas breakfast, described above. At the end of five hours after the first meal, that is to say,

one hour after the second, the gastric contents is withdrawn.

The Salzer test affords, in addition to the opportunity of ascertaining acidity, that of determining the motility of the gastric muscles; for if particles of meat of the first meal are still present at the end of five hours, the propulsive activity of the stomach wall is deficient.

Withdrawal of Gastric Contents.—This, the next step of the examination, is carried out with the aid of a flexible red rubber tube about a yard in length, the catheter-like end of which is provided, a short distance above the tip, with a fenestra or opening. It is an ordinary stomach tube the upper end of which is funnel-shaped. About 2 feet above this end is a mark which, when the tube is introduced sufficiently far, *i.e.*, when its tip reaches the bottom of the stomach, corresponds with the incisor teeth of an adult.

The patient's clothing being protected with a towel tied round his or her neck, the tube, previously warmed by being placed in a bowl of warm water and lubricated with glycerin, is introduced, *i.e.*, passed down the esophagus. This is done readily by pushing the end of the tube gently into the latter, over the epiglottis, while the patient swallows, and as often as he does so. In some cases, especially the first time, the procedure may cause gagging, but this can be avoided by passing the tube on one side of the epiglottis, *i.e.*, in either pyriform sinus. The sensitive surface of the pharynx is thus avoided.

To withdraw the gastric contents several ways are available. The easiest is to depress the external end of the tube as soon as the latter is *in situ*, and request the patient to lean forward and cough a few times or contract his abdominal muscles. An essential point, however, is that the (clean) bowl in which the gastric contents is to be collected must be considerably below the level of the patient's stomach, *i.e.*, between his knees, so as to obtain the benefit of siphonage. The expulsion of the gastric contents is facilitated by pressing on the stomach while the patient is coughing or contracting his abdominal muscles; it is further aided by having him lie down on a lounge, the bowl being placed on the floor. It is not necessary to

empty the stomach, a couple of table-spoonfuls (about 30 c.c.) sufficing for all purposes.

Various pumps, aspirating bulbs, etc., have been invented to deplete the stomach, but they entail the use of parts that are difficult to clean properly, and expose the gastric mucosa to the evil effects of direct suction by the tube. Moreover, complicated instruments tend to increase the timidity of the patient, which, at best, is sometimes difficult to overcome. Briefly, the above-described "simple expression method" is, on the whole, the most satisfactory.

Contraindications to the Use of the Stomach Tube.—In a certain proportion of cases, however, even the use of the simple stomach tube may prove dangerous. They are: cases of advanced cardiac disorder; advanced arteriosclerosis, especially if there is a history of cerebral hemorrhage or "slight stroke"; elderly persons of apoplectic build. In either of these the tube may cause a sudden reflex rise of the blood-pressure and rupture of any diseased vascular tissue. A history of recent hematemesis or of bloody or tarry stools is also a contraindication, since the bleeding may be due to gastric ulcer or cancer, which the extremity of the tube might readily abrade, and thus cause renewal of the hemorrhages. Advanced tuberculosis, marked emphysema, pregnancy, and extreme debility are also recognized as contraindications.

Determination of Free Acids.—The mere presence of any free acid, hydrochloric, lactic, etc., can readily be determined by using paper previously dipped in a solution of *Congo red* and dried. This turns blue in the presence of free acids, but does not identify one acid from another.

To identify hydrochloric acid, the best reagent is probably the *dimethylamidoazobenzol.* It may be used in 0.5 per cent. solution or in absorbent paper allowed to dry before using. The yellow color of either becomes reddish pink in the presence of hydrochloric acid. This test furnishes an inkling as to the degree of acidity due to the latter, for the reddish-pink color becomes much deeper in proportion as the percentage of acid is great.

Tropeolin is another good reagent which can be used in the same manner. Its yellowish-brown alcoholic solution turns red in the presence of both hydrochloric acid and lactic acid; but the former can be differentiated by spreading a few drops of a saturated solution in a porcelain dish, and adding thereto an equal quantity of the gastric fluid. On mixing them and heating them gently, blue and lilac stripes (formed by hydrochloric acid only) appear.

An extremely delicate test, which will detect 1 part of hydrochloric acid in 20,000 parts of water, is *Gunzburg's,* whose reagent consists of:—

R *Phloroglucin* .... 2 Gm. (30 gr.).
   Vanillin .... 1 Gm. (15 gr.).
   Absolute alcohol ...... 30 c.c. (1 oz.).

It should be kept in a dark bottle. By adding a few drops of this reagent to the gastric filtrate and allowing the mixture to evaporate to dryness, a beautiful rose-red tinge is obtained if free hydrochloric acid is present.

To Ascertain the Total Acidity.—The easiest method is to add 1 drop of a 1 per cent. solution of *phenolphthalein* to 10 c.c. (2½ drams) of the gastric fluid, after filtering the latter, and neutralizing the mixture by a given quantity of decinormal solution (about 30 grains to the pint—2 Gm. in 500 c.c. of distilled water) of sodium hydroxide. The technique of the procedure is as follows: Place 10 c.c. of the filtered gastric fluid in a beaker, and add thereto 2 drops of phenolphthalein solution. Then add the decinormal sodium hydroxide solution from a *graduated* burette (mixing with a glass rod) until a permanent red or reddish-pink color appears, which means complete neutralization. Now, the number of c.c. (say 4 or 4.5) of sodium hydrate solution necessary to obtain the latter, as shown by the graduated burette, with a naught to the right of this figure (making 40.0 or 45.0 of the above figures), will represent the percentage of total acidity.

A watery solution of Congo red may be used instead of phenolphthalein. As we have seen, free hydrochloric acid in the gastric fluid or chyme changes the red color to blue. If, now, decinormal sodium hydrate solution (*vide supra*) is slowly added to the mixture until the Congo red

is restored, the number of cubic centimeters of the sodium hydrate solution required to obtain this result will represent the amount of free hydrochloric acid.

Lactic acid, which suggests the presence of cancer or dilatation, being contained in all bakery products, in meats as sarcolactic acid, sour milk, sauerkraut, and sour gherkins, a special meal is necessary to eliminate from the test the acid due to
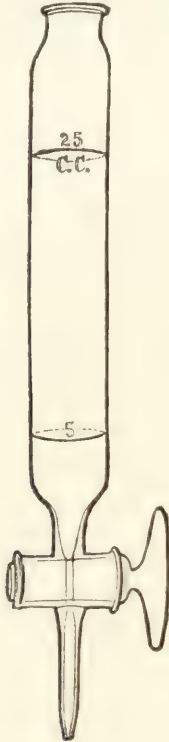
Strauss's separating funnel for lactic acid test.

foods. A bowl of soup prepared with Knorr's oatmeal, rendered palatable by adding common salt, suffices for this purpose. *Uffelmann's reagent* may then be used. It is composed as follows:—

℞ *Solution of carbolic acid* (4
    per cent.) .... 10 c.c.
Distilled water .... 20 c.c.
Official neutral ferric chloride
    solution .... 1 drop.

This should be prepared fresh for each test. Its amethyst-blue color will be turned to canary yellow when added to the gastric filtrate.

A quantitative estimation of lactic acid may be obtained by *Strauss's method.* "A separating funnel (shown in the annexed cut) with marks at 5 c.c. and 25 c.c. is filled to the first mark with gastric juice and then to the second with ether. After thoroughly shaking, the fluid is allowed to flow out to the first mark (5 c.c.), then filled with water to the second mark (25 c.c.). Two drops of a 10 per cent. solution of iron chloride are then added. A beautiful green color appears in the presence of amounts exceeding 0.5 per mille." (Lenhartz-Brooks.)

Butyric acid and other fatty acids, on boiling the gastric filtrate, emit a characteristic odor. They also turn yellowish brown in the presence of *Uffelmann's solution,* just described. Another test is to shake the gastric product (unfiltered) with acid-free ether, and then allow the latter to evaporate. On adding *calcium chloride* to a watery solution of the residue, the butyric acid forms oil droplets with the characteristic odor of the acid.

Acetic acid also emits a characteristic odor, that of vinegar. A small quantity of gastric filtrate, say 10 c.c., is treated with ether as above. The residue being dissolved in a little water and neutralized with a solution of sodium carbonate, a couple of drops of a very dilute solution of ferric chloride are added. The filtrate then becomes dark red if acetic acid is present. Or a few drops of sulphuric acid and alcohol may be added to the same neutralized residue; on heating, the latter then gives off the characteristic vinegar-like odor of acetic acid.   S.

ACIDOSIS. See AUTOINTOXICATION.

ACNE.—DEFINITION.—Acne

is characterized by the presence, usually on the face, of small elevations or nodosities varying in size from a pinhead to a pea. These elevations, or pimples, are also present on the back, shoulders, and chest in many cases.

SYMPTOMS.—The elevations are conical or hemispherical, and, as a

rule, in the earliest stage of the lesion somewhat painful, especially upon pressure. In most of the lesions there is a distinct tendency to suppurative change. In the center of the lesion a whitish-yellow spot forms where the pus raises the epidermis. In from three to ten days, or even longer, the lesion breaks and a small amount of pus is discharged. At other times the pus dries to a thin crust, or occasionally the contents, especially in sluggish lesions, are absorbed. A red elevation is left which gradually flattens out, leaving a brownish stain, which eventually disappears. The surrounding skin is frequently oily and shiny. Small, sluggish, abscess-like lesions, and tumors as large as a pea or a small nut, formed by retention cysts of sebaceous glands, are sometimes seen; they may gradually work to the surface or may persist for months and finally disappear or form hard spherical indurations by retraction and inspissation of their contents. Scarring, usually consisting of small, white, cicatricial depressions, is to be seen as a consequence in some cases. In the majority of cases, however, permanent marks are not left. The regions most affected in acne are the face, shoulders, and anterior and posterior aspects of the shoulders. Occasional cases are observed in which the back, extending as far down as the sacrum, is the chief seat of the disease. In rare instances (acne cachecticorum, acne scrofulosorum, and acne medicamentosa) the eruption may be more or less general.

VARIETIES.—There are several varieties of lesion observed in acne, one kind of which is apt to predominate, and this has given rise to the so-called varieties of the disease.

Acne vulgaris, or *acne simplex,* is, by far, the most common clinical type. The lesions are usually of a mixed character, consisting of blackheads, pinhead- to pea-sized papules, papulo-pustules, and pustules. Each lesion may in its beginning have a small, red areola. There is also slight pain upon pressure. The lesions are rapid in evolution, running a course in several days to a week. As in all types, they are discrete and isolated.

The term *"acne papulosa"* is given to a not uncommon type in which the lesions are usually small and show but little disposition to reach the pustular stage, disappearing by absorption or by desiccation and exfoliation.

Acne punctata might be termed minute papular, the lesions being, for the most, pinhead in size, with a central comedo, or blackhead.

Acne pustulosa is another type in which the lesions go rapidly into the pustular stage, the eruption appearing, for the most part, to be made up, almost entirely, of pustules. In size they vary from a large pinhead to a large-sized pea.

Acne indurata, or *"tuberculosa,"* is a form of the eruption in which the lesions tend to be closely crowded here and there and in such places, and also with single lesions, the underlying base becomes hard, inflamed, and indurated, being also somewhat deep-seated.

In *acne phlegmonosa* the inflammatory and suppurative process begins deep down in the sebaceous gland, forming veritable small dermic and intradermic abscesses, usually with but slight tendency to break through the surface.

Acne cachecticorum characterizes an acneic eruption, more or less general,

occurring in weak, cachectic individuals; the lesions are livid, indolent, violet-red papulopustules of moderate and large size and of slow evolution, leaving, as a rule, small cicatrices. Acne scrofulosorum is really a variety of the last named,—acne cachecticorum,—occurring in those of distinctly strumous or tuberculous temperament.

Acne artificialis seu medicamentosa is a form of acneic eruption produced by the ingestion of certain drugs, as the iodides and bromides, and also by the external applications of certain remedies, such as tar, the paraffin oils, etc.

"Acne atrophica" is a name given to those cases of acneic eruption which tend to leave depressed scars. This probably occurs most frequently in those cases in which the lesions are sluggishly papular or papulopustular, the lesions disappearing by absorption or crusting and leaving behind small, punched-out cicatrices.

Acne hypertrophica is really the opposite of the last-named variety, and occurs in about the same kind of cases, small, whitish, connective-tissue, pinpoint or small-pea sized projecting hypertrophies marking the sites of the lesions. It is rare.

ETIOLOGY.—Acne begins usually near puberty, when the pilar system is more actively developing, and the functions of the sebaceous glands likewise; and is more frequent among patients with digestive troubles, constipation, dilatation of the stomach, menstrual irregularities, the strumous diathesis, possibly the arthritic diathesis, and disturbances of the nervous system.

The etiological participation of gastrointestinal disorders in acne vulgaris are receiving due attention.

While the acne bacillus is generally recognized as the direct cause of acne vulgaris, a number of associated conditions probably act as predisposing factors, among which gastrointestinal abnormalities seem of special importance. They investigated the problem in 30 cases by means of fluoroscopic examination of the gastrointestinal tract, test meals, and analyses of the gastric contents. It was found that 93 per cent. showed gastric abnormalities and 70 per cent. intestinal abnormalities. The most common gastric findings were hyperacidity, 48.1 per cent.; retention, 36.6 per cent.; atony, 33.3 per cent., and ptosis, 40 per cent. The most common intestinal findings were cecal stasis, 46.6 per cent.; ptosis of the colon, 36.6 per cent., and right lower quadrant adhesions, 23.3 per cent. Clinically, 62.3 per cent. of the cases gave evidence of gastric disturbances and 40 per cent. were constipated. None of the cases examined gave entirely normal gastrointestinal findings, and 60 per cent. showed abnormalities which were of such a nature as to permit gastric and intestinal stasis, followed by toxic absorption. L. W. Ketron and J. H. King (Jour. Amer. Med. Assoc., Aug. 26, 1916).

[The confusion concerning the pathogenesis of acne is due, in my opinion, to the fact that the *ductless glands* are overlooked in the morbid process. As I pointed out in 1914 before the Manhattan Dermatological Society of New York, a close relationship suggests itself when these structures are accepted as active participants in the morbid process. At puberty we encounter the period when the thymus has ceased to furnish its nucleins. Many of the disorders of adolescence may be traced to this cause. Development has ceased, and the other or permanent ductless glands whether ready or not, must sustain the life process without the thymus. The pancreas, thyroid and adrenals maintain not only the nutritional processes of the body, oxidation and metabolism, but simultaneously its defensive process. When we realize that they do this while carrying out the catabolic

phase of metabolism, and as a part of this process, breaking down poisons, toxins, etc., as they do normal wastes, the apparent complexity of the immunizing process disappears. Nevertheless, upon the integrity of these two connected functions depends the health of the whole.

Many other facts submitted at the time suggest that acne may be due to inadequate defensive activity of the body through insufficiency, inherited or acquired, of one or more of the ductless glands, which not only from my viewpoint nowadays, but from that of others, take part in this general defensive process. We have indirect proof of deficient immunizing power as a cause in the effectiveness in many cases of acne, of **staphylococcus vaccine,** which though not specific, nevertheless provokes the formation of antibodies. **Thyroid gland** with **pituitary** or **ovarian gland** is also effective in hypothyroidism, especially hypothermia are discernible.

When, as stated above, gastrointestinal disorders exist in the case, the resulting autointoxication aggravates and may doubtless cause the disease, owing to the deficient antitoxic activity of the blood, due in turn to the deficient activity of the ductless glands. C. E. DE M. S.]

It has been also alleged without, however, substantial foundation that lesions of the genitourinary organs and venereal excesses may provoke the disease. Lesions may be due to mechanical irritation caused by the product of secretion remaining in the excretory canal or gland itself. Some drugs, as already stated,—such as the bromides and iodides,—are occasionally responsible for the eruption or an increase in an already existing eruption. Certain drugs applied externally may also provoke acneic lesions, such as tar and tar products, juniper oil, and the like. Workers in paraffin and paraffin products will not infrequently be found affected with papules and pustules, especially those of a furuncular or abscess type. The direct local exciting factor is thought,

by many, to be a micro-organism, Gilchrist's observations pointing to a specific bacillus.

PATHOLOGY.—In most cases the process begins by a perifolliculitis, which later on gives rise to a purulent folliculitis. It would thus seem that in some cases the sebaceous glands play but a small part in the affection. In most cases, however, when comedones are present, the sebaceous gland itself is the starting point of the inflammatory process. (Brocq.)

Even when the focus of irritation is in the follicle, it is frequently limited to the sebaceous or sebaceous pilary canal. (E. Besnier, A. Doyon.)

The papillæ surrounding the comedone and the superficial layers of the corium are filled with blood-vessels full to repletion, and of exudation cells which are found in dilated vacuoles. (Kaposi.)

If the process is very intense, the sebaceous gland may be entirely destroyed by the local inflammatory action, while the pilar bulba persists. (Kaposi.)

The acneic process may be divided into two parts: 1. Closure of the sebaceous follicle and formation of comedo. 2. Suppuration, which only occurs in those follicles where the staphylococci aureus et albus have penetrated before the comedo formed.

The complement fixation reactions tended to show the activity of colon bacilli in certain skin diseases, particularly acne vulgaris, rosacea, and seborrheic dermatitis. Almost two-thirds of the cases of acne gave a positive complement fixation test with the *Bacillus coli* obtained from the feces of acne patients. In contrast to this, only 15 per cent. of non-acneiform skin affections gave positive reactions with this bacillus, and the non-eruptive controls which were

examined gave entirely negative re-
sults with this organism. With a
polyvalent antigen of strains of colon
bacilli recovered from the feces of
persons suffering from acne vulgaris,
the percentage of positive reactions
and the degree of complement ab-
sorption were found to be higher
than with the control antigens of
colon bacilli from the feces of normal
persons, with the sera of persons suf-
fering from acne vulgaris and sebor-
rheic dermatitis. Kolmer and Scham-
berg (Jour. Cutan. Dis., xxxiv, p.
166, 1916).

TREATMENT.—In this connec-
tion acne may be divided into (1) an
irritable or inflammatory variety, in
which the skin is fine and thin and
easily irritated by stimulating applica-
tions, and where general treatment is
important on account of the close
union between the acneic eruption
and various constitutional disturb-
ances. Local treatment should, at
first at least, be of a mild character.
(2) An *indolent* variety, where the in-
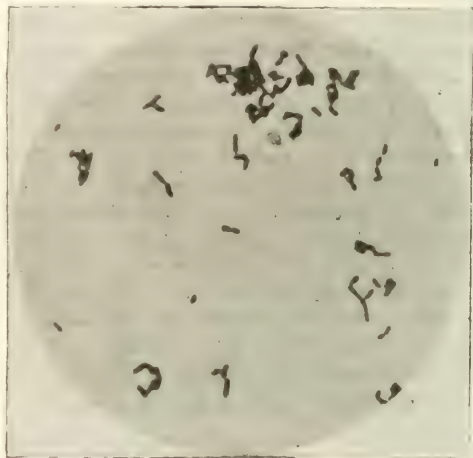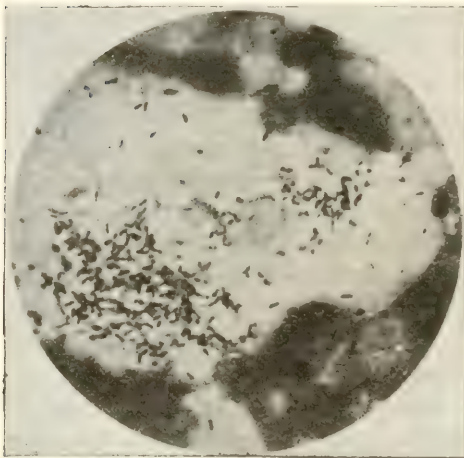
Bacillus acnes (*Hartwell and Streeter*).
Boston Medical and Surgical Journal, Dec. 16, 1909.

DIAGNOSIS.—Acne is to be dif-
ferentiated from the papular, papulo-
pustular, and pustular syphiloderms,
and also from variola.

Syphilis.—In the syphilitic eruption
the distribution is more or less general,
and more acute in its outbreak, darker
hued, and occurring occasionally with
special groupings and the presence of
other symptoms of the disease.

Variola.—In small-pox the premoni-
tory constitutional symptoms, the sud-
den outbreak, the uniformity of the
lesions, and many other symptoms of
differential character will serve to
differentiate.

tegument is thick, rough, and oily, with
enlarged and obstructed gland orifices,
and where the most energetic local ap-
plications are well borne; here the local
treatment is important. Probably
most of the cases met with occupy a
middle ground between these two ex-
treme varieties.

General Treatment. — Prophylactic
measures, such as the avoidance of ex-
ternal irritants, drugs and food liable
to cause acne, such as coffee, tea,
alcohol, pure wine, pork, veal, game too
far gone, preserved fish, shellfish, fats,
and cheeses.

Any disorder of digestion must be

counteracted in order to avoid the congestion of the face following meals.

If the tongue is much coated and shows prominent papillæ, the following is recommended:—

> ℞ *Sodium bicarb.* .... 10 grs.
> *Ext. cascara sagr. liq.*.... 10-20 mins.
> *Tinct. nux vomica* .... 7-10 mins.
> *Peppermint water*..to make 1 fl. oz.—M.

Constipation should be counteracted by gentle **aperients**. Any condition capable of maintaining the sympathetic system in a state of tension—such as genitourinary troubles or affections of the nasal fossæ—should be eradicated if possible.

If the patient is lymphatic and has a good digestion, **codliver oil** is of value.

Anemia or chlorosis calls for the use of **chalybeates** with **arsenic**. Iron often does harm unless its constipating effect is counteracted by using aperients. When the patient is arthritic, **alkalies**, especially alkaline waters, are indicated.

No really specific treatment is known against acne, but the following have been recommended:—

Sulphur alone: powder or tablets, or with equal parts of honey.

Ichthyol (Unna) :—

> ℞ *Ichthyol* .... 1-2 drs.
> *Dist. water* .... 5 drs.

M. Sig.: Fifteen to 50 drops in water, to be taken morning and evening.

Arsenic bromide in weak doses, $\frac{1}{60}$ grain, in acne pustulosa. (Piffard.)

Mercurial preparations, such as **corrosive sublimate** or **calomel**, either alone or with **jalap** or **colocynth extract**, have been found useful.

> Summary of treatment: Prohibit cakes, pies, pastries, salt meats, fish, and eating between meals. If anemic, give nourishing foods. **Ferri citratis**, ℥ij; **magnesii sulphatis**, ℨv; **strychninæ**, gr. j; syr. zingiberis, ℥j; aquæ,

℥iv. In obese, constipated, and sluggish individuals: **Potassium acetate**, ℨv; fl. ext. of **cascara sagrada**, ℥ij; fl. ext. of **rumex**, ℥iij; 1 dram in water half-hour before meals. **Outdoor exercise.** Where comedones or pustules: **Green soap**, ℨj; **resorcin**, ℨj; **salicylic acid**, gr. v; **rose-water ointment**, ℥ij; to be applied at night and washed off in morning, until fair desquamation obtained. Lotio alba (**potassium sulphide and zinc sulphate**) applied at night after using hot or cold water; friction with towel. Cocks (Med. Record, Dec. 3, 1910).

Acne vulgaris is caused principally by 2 factors: eating fermentable foods, and inability to prevent such foods from fermenting. Menstruation, cigarette smoking, anemia, etc., are factors in acne through their influence on digestion. The treatment consists in **thorough mastication** of the food, putting the **teeth in good order**, and **excluding starches and sugar** from the diet. Antifermentive drugs, such as **aloin** 0.1 Gm. (1½ grains), **ichthyol** 10 Gm. (2½ drams), licorice powder q. s., to be mixed and divided into 30 capsules and 1 taken after meal, are of value. **Sunlight** and **fresh air** as well as exercise help a great deal. Drying and peeling lotions help locally. **Vaccines** often control the formation of pus in the lesions, but cannot, in the writer's opinion cure acne vulgaris. R. A. McDonnell (Jour. Cutan. Dis., Feb., 1917).

The writer recommends in the treatment of acne, in addition to the customary local and dietetic measures, **suprarenal gland** 5 grains (0.3 Gm.), given 3 times a day.

In cases showing torpidity he advocates **thyroid gland** ¼ grain (0.016 Gm.), thrice daily. **Ovarian** and **testicular extracts** are also commended. Hollander (Arch. of Derm. and Syph., May, 1921).

Local Treatment. — Constitutional treatment will rarely succeed alone, while in a large proportion a local treatment by itself will be found efficacious.

The condition of the skin should be improved so that it will no longer be a suitable culture ground for the bacillus. The follicles of the skin should be emptied of the colonies of bacilli. The skin should be constantly kept aseptic, so that any bacilli that escape on it will be killed, and no new infection of the skin will be possible. The first indication is met by attention on the patient's general health by means of baths, diet, exercise, attention to hygiene, and lastly, drugs. The follicles are emptied by the use of the curette, the acne lancet, and the comedo expressor. The best local application is **sulphur**, preferably in the form of the old lotio alba, the formula for which is: **Zinc sulphate** and **potassium sulpheret**, of each, ʒi-ij; **rose water**, q. s. ad ℥iv. This is to be shaken up before using. **Resorcin** is also useful, as well as **sulphur soap.** The use of the **Röntgen ray** should be limited to intractable cases, and requires great caution to prevent doing harm. G. T. Jackson (Med. Rec., Mar. 18, 1905).

Hot-water and **alcoholic lotions** sometimes act promptly. In mild cases these are applied at night with very hot water, either pure or combined with **cologne water** or **camphorated alcohol.** The water is gradually reduced until pure camphorated alcohol or cologne water is used. **Boric acid** or **borax** may be added to the lotions: 1 part to 50.

Night and morning the skin should be bathed in very **hot water** (to reduce the congestion), to which **creolin,** or a few drops of the following solution, should be added:—

℞ *Corrosive sublimate* ....   7½ grs.
  Tinct. of benzoin ....   75 grs.
  Emulsion bitter almonds. 3675 grs.
M.

E. Lacour (Nord méd., Aug. 15, 1900).

Many of the less severe forms can be cured by prolonged **bathing in hot water.** The water should be soft, and the applications to the face should be made with a soft bathing sponge. The sponge, loaded with water as hot as

can be borne, should be applied to the face. The bathing should last about five minutes, and should be done each night and morning; at the same time moderate pressure is applied to the sponge. After the sponging the face should be dried on a soft towel without rubbing, and **bay rum** should be applied freely. The face should not be touched by the hands until the time for repeating the process. W. L. Hunt (Jour. of Med. and Sci., Sept., 1904).

Have patient vigorously scrub his face, every night before retiring, with **green soap** and **hot water**. After rinsing with cold water and drying the face, the following paste is to be applied: **Betanaphthol,** 5 parts; **precipitated sulphur,** 25 parts; **green soap** and **lanolin,** of each, 35 parts. Spread this over the involved area and allow it to remain fifteen minutes to one hour, after which it is wiped off. Length of application depends on the reaction produced; if left on too long, the skin reddens, or, after greatly prolonged contact, the epidermis desquamates. This paste acts probably by causing an inflammation of the skin, which extends along the dilated follicles, thus inhibiting the secretion and producing shrinkage of the dilated sebaceous glands. When the condition is improved, continue the applications at longer intervals to prevent recurrence; also scrub face every second or third night. Burke (Penna. Med. Jour., March, 1911).

Instead of camphorated alcohol there have been used with success:—

Alcohol, 96°, saturated with **boric acid,** and **alcohol** with **salicylic acid,** 1 to 30. The latter is strong and must be used with care.

Mercurial preparations have been variously extolled, but in late years have gradually given way to other more valuable remedies.

Mercurial lotions are efficacious in some cases, employed as follows:—

℞ *Corr. subl.* ....   1 part.
  Alcohol, 90° .... 100 parts.
  Dist. water or *rose water* ... 150 parts.

At first this solution is weakened with one-half its quantity of water; afterward, if no irritation has resulted, the water is gradually reduced until the solution is employed pure.

Other **mercurial preparations,** in ointment form, such as the biniodide, the iodochloride, white precipitate, and mercurial plaster, viz.:—

The **ammoniated mercurial ointment,** 5 grains, or 30 grains to 1 ounce, is highly recommended by Stopford Taylor.

Gordon Campbell recommends the following procedure :—

The face is to be washed with water as hot as can be borne and some bland unirritating soap, and then, after carefully drying the skin, the following lotion is applied once a day :—

> R *Hydrargyri chloridi corrosivi.* 12 grs.
> *Spiritus vini rectif.* .... 6 oz.—M.

Effect for first few days will be to render condition worse; but, after this, the lotion prevents perforation of the pustules.

> External drug treatment in both acne vulgaris and acne rosacea is usually disappointing. **Sulphur** is the best external preparation. Mechanical treatment, such as the use of **hot water, soap, massage,** and the **dermal curette,** is exceedingly valuable. The **opsonic method** in acne vulgaris is promising. **Roentgen treatment** of both diseases is the most valuable. In its certainty of cure and frequency of relapse it almost approaches a specific. The technique of using the X-ray, say, in acne, is of paramount importance. If the ray is properly applied there should be few, if any, failures and no undesirable effects. Cole (Jour. Indiana State Med. Assoc., Mar., 1909).

Formaldehyde, largely diluted, has recently been tried with success.

Sulphur preparations are by far the most valuable in the external treatment of the disease; especially useful when much seborrhea exists. In a few patients sulphur preparations cannot be used, owing to the irritation caused. Sulphur may be employed in the following ways :—

Sulphur soap: with hot water, the suds being allowed to dry on to the face.

Sulphur baths.

Sulphur lotions: hot water with 10 to 60 drops for every one-half glassful of liquid **potassium polysulphide.**

An effective method of using sulphur is the following :—

After washing with hot water and soap, the following mixture is applied with a camel's hair brush :—

> R *Precipitated sulphur,*
> *Potassium bicarbonate,*
> *Glycerin,*
> *Laurel water,*
> *Alcohol* (60°) ......of each 2 drs.—M.

The coating is left on during nighttime and washed off in the morning with an **emulsion of almond oil,** and the skin is covered with **oxide of zinc** or **bismuth subnitrate ointment** powdered over with fine starch.

When the skin becomes irritated, the sulphur paste should be discontinued and the **zinc ointment** applied alone until the irritation has disappeared.

The following are useful :—

> R *Sulphate of zinc,*
> *Sulphuret of potassium.*.of each 1-4 drs.
> *Water* .... 4 oz.

> R *Precip. sulphur,*
> *Ether* ....of each 4 drs.
> *Alcohol* ....to make 4 fl. oz.

> R *Precip. sulphur* .... 2 drs.
> *Gum tragacanth,*
> *Camphor* ....of each 20 grs.
> *Lime water* .... 2 fl. oz.
> *Water* ....to make 4 fl. oz.

Both these lotions are often made more valuable by the addition of 2 to 5 per cent. of **resorcin.**

Sulphur ointments are usually made in the proportion of 1 in 10, with benzoated lard, simple cerate, vaselin, vaselin and lanolin, lanolin and sweet almond oil or olive oil, or castor oil and cacao butter.

To the sulphur may be added **oxide of zinc** in equal parts; borax, 1 to 20; **salicylic acid,** 1 to 50; **naphthol,** 1 to 10 or 1 to 20; **resorcin** or **camphor,** 1 to 20 or 1 to 40. They may be perfumed with essence of rose, bergamot, or balsam of Peru if desired.

Sulphur soaps are sometimes more convenient.

The following may be used :—

Soap and precipitated sulphur, equal parts.

Soap, precipitated sulphur, and lard, equal parts.

Naphthol may be cautiously added to the first of the series.

Among other local treatments recommended are the application to the pustules of **carbolic acid, salicylic acid, or resorcin.** An ointment of **ichthyol,** 1 to 4 or 1 to 8, is also useful.

The following **resorcin paste** is recommended :—

R *Resorcin* .... 2½-5 parts.
  Zinc oxide,
  Starch ....of each 5 parts.
  Vaselin .... 12½ parts.—M.

This paste may remain on a day and a night and then be removed with a piece of cotton. Cure is said to be speedy, occurring in three or five days. It is a strong preparation, acting with considerable energy in some cases.

In slight cases of acne of the face the following formula is recommended: **Eau de cologne,** or 90 per cent. alcohol, with **resorcin** or **salicylic acid,** 2 to 4 per cent., or sublimate or **cyanide of mercury.** After these lotions the skin should be slightly greased with **lanolin,** 10; **water,** 20; and **rose water,** 5 parts. The application of an aqueous solution of **ichthyol,** 5 to 10 per cent., is also useful. Leredde (Bull. gén. de thérap., 1903).

Salicylic acid acts well in from 1 to 2½ per cent. in various ointments.

Electrolysis has been recommended for the removal of the indurated masses left on the skin.

In acne of the back the strongest applications, as a rule, are demanded. Of especial value in some cases is the **liquor calcis sulphuridis (Vleminckx's solution).** This should be used at first diluted.

Massage of the face is not to be commended for acne, often doing distinct harm.

The comedo is in the majority of cases the forerunner of the acne nodule and pustule. The comedo is best removed by a comedo extractor, which should have rounded edges. The pressure should be moderate, and if the comedo does not escape it is best to puncture with a narrow bistoury. This should be done by the physician. The papules and pustules are treated by **lancing.** When more active methods are not employed, it is of value to cover the parts with **mercurial plaster** for a few nights. Various useful methods have been devised, the main local applications consisting of **sulphur, salicylic acid, resorcin,** and **soap.** The best treatment, however, is the **X-ray.** In many cases irradiations will obviate the necessity of lancing the nodules and pustules. D. Lieberthal (Lancet-Clinic, Dec. 30, 1905).

Before undertaking the local treatment of acne it is well to **open the pustules, empty the comedones** and sebaceous cysts, etc. These measures often prove satisfactory in indurated and rebellious acne. Some observers

object, however, to the use of the curette.

Facial acne gives favorable results under treatment by a **glass vacuum electrode excited by the Oudin resonator** and transmitting quite a strong current. The bulb should be rubbed over the skin without breaking the contact, and at the same time a constant stream of tiny violet sparks should pass from parts of the bulb not in the closest contact with the skin. The face should be somewhat red after an application lasting six or eight minutes during which the electrode is in constant motion. The writer is most strongly opposed to the practice of opening acne pustules. He has seen faces as badly marked as by small-pox. It seems much better to treat the case along the following lines: **Rhubarb and soda** internally relieve any source of irritation, such as phimosis; cleanse the skin by vigorous **washing with tar soap** every night and then apply a soothing antiseptic salve, such as **ung. zinci oxidi**, 2 ounces (62 Gm.); **pulv. acidi salicyl.**, 20 grains (1.3 Gm.). This treatment combined with that by **high-frequency currents** has enabled the author to permanently cure a number of cases of acne vulgaris and the disagreeable and intractable acne rosacea. Sinclair Tousey (Amer. Jour. of Dermat., Oct., 1911).

Mild **X-ray** exposures of short duration and low vacuum may often be advantageously employed, but should be done with great caution and as an aid rather than the sole measure of treatment. Its indiscriminate and injudicious use is to be condemned.

In the majority of cases repeated small doses of **X-rays** will bring about a satisfactory cure, even when all other treatments have completely failed. A third of a Sabouraud's pastille dose repeated at the end of a week, and then after fourteen days, is the system found to agree best in most cases. After this it is often desirable to keep up the effect of the

rays for a considerable time, at three weeks' to a month's interval, between applications. Sibley (Clinical Jour., Apr. 29, 1914).

Repeated small doses of the X-rays not strong enough to induce appreciable reaction in the skin, or a single large dose with a reaction, seem to be able to modify the sebaceous glands to such an extent that the tendency to acne dies out. This proved true in a large number of cases. Its efficacy is greater in acne spread over a larger surface, with numerous pustules, than in the less disfiguring, torpid type. Dosseker (Therap. Monats., Aug., 1915).

Dietetic measures are unnecessary. He removes all oil excess by **pure alcohol cleansing** of the face, the **copious water drinking** and **X-ray** 5 minutes to each side once a week, or if erythema occurs every other week. Le Fèvre (Ohio State Jour. of Med., Feb., 1917).

The writer recommends the judicious use of the **X-ray** in acne. The nodular and keloidal varieties are not otherwise amenable to relief. Relapse after apparent cure by X-rays is rare. Should it arise it can be dealt with by further irradiation. Semon (Brit. Med. Jour., May 22, 1920).

According to Bier, nature always meets a pathogenic substance with the same weapon, namely, **hyperemia**. This is shown either by scratching a sterile skin with a sterile needle or by infecting any organism with any irritating or poisonous germ, or, most commonly of all, by the reaction of the part when a small splinter is lodged in the skin. The object is to increase the local blood-supply. Bier's method has been tried in acne with some success.

Bier's method for the treatment of acne consists in the application of dry cups to the affected region for one-half hour once or twice a day. The suction is slight, and the cup is removed and reapplied every one or two minutes. From two to five ap-

plications must be made over the same area before improvement is effected. The method does not prevent the appearance of new pustules, though they become less frequent. Eight cases treated by this method alone produced marked improvement. Moschowitz (Med. Rec., Jan. 13, 1906).

Bier's suction cups found useful. Applied for repeated five-minute periods with three-minute intervals, making two to five applications at each *séance*. Sibley (Lancet, Feb. 4, 1911).

Sir A. E. Wright's **vaccine therapy** has also been used with success in acne. As this investigator explains, no attempt is made to supply to the patient protective substances produced in the organism of an animal vicariously inoculated, but the chemical machinery of the patient is induced to elaborate by its own efforts the protective secretion which is required for the destruction of the pathogenic agent.

> Severe cases of acne often do better under **vaccine** treatment than comparatively mild ones; the most resistant to this treatment are usually those with abundant seborrhea, many comedones, and scanty foci of suppuration. Vaccine treatment must be continued for 6 months at least, and long after all spots have ceased to appear, when diminishing doses at longer intervals will often prevent relapses and complete a cure. Sibley (Clinical Jour., Apr. 29, 1914).
>
> In Cornell University it was found that entering students showed 30.2 per cent. of the freshman class suffered from acne vulgaris; general in 17.8 per cent., and limited to the face in 12.2 per cent. Their treatment showed the superiority of well-known therapeutic measures over vaccine therapy. Indeed, T. J. Horder has well said: "The failures of vaccine therapy are probably more numerous than its successes." Fox (Jour. Amer. Med. Assoc., June 24, 1916).

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ACNE BACTERIN. See BACTERIAL VACCINES.

ACNE ROSACEA.—DEFINITION.—Acne rosacea is characterized by a chronic congestion of the face, causing vascular dilatations; and by changes in the cutaneous glands and tissues, giving rise to seborrhea, inflammatory acne, and hypertrophic changes.

SYMPTOMS.—The nose and malar eminences are especially prone to this disorder. It may also affect the forehead, chin, the neighborhood of the alæ nasi, the cheeks, and less commonly the side of the neck. In women the chin is occasionally invaded.

There are three forms of acne rosacea.

The first is the *erythematous and telangiectasic*. It may be characterized by temporary congestive spots on the face, showing themselves especially after meals and in the evening. These spots may be accompanied by no other lesion. This form is usually present in connection with more or less seborrhea, especially on the nose, which is generally very oily. Again, the erythematous variety may be characterized by small vascular dilatations on the nose or malar eminences, which dilatations develop gradually, unite with one another, and form a network. This network is uniform in hue at a distance, but nearby may be seen to be formed of congested surfaces over which are spread vascular dilatations. This degree of the erythematous form is almost always accompanied by seborrhea, enlarged nose, and dilated glandular orifices, especially in women toward the menopause and in wine-drinkers.

The nose may be slightly violet hued and be cold to the touch.

The second form is the *erythematous* acne, or *true acne rosacea*. In addition to the erythematous and congestive feature, there may be found in this variety a true acneic and acne-like element: papules, pustules and tubercles or nodules. In some cases the acne appears before the congestion. There is a congestive red base with fine vascular dilatations and papulopustules of various sizes, often resting on an indurated violet-red base.

In this variety there may also be increase in number and size of the vascular dilatations, increase in size and depth of the acneic indurations, and proliferation and hypertrophy of the derma.

The third form is the *hypertrophic* acne, or *rhinophyma*. In this variety the glandular orifices are much enlarged, while the glands themselves may be ten to fifteen times increased in size. The tissues around them proliferate, forming a variety of pachyderma. The nose may be red or violet hued, covered with enlarged orifices, greatly increased in size, occasionally reaching considerable dimensions (the so-called Pfundnase of the Germans). Its exterior may be mammillated. (Brocq.)

Two subdivisions of this form are rendered necessary by the difference in the pathology of each. The first, glandular, presents an embossed aspect, the hypertrophy being due especially to hypertrophy of the pilosebaceous glands; the second, elephantiasic, presents a smooth aspect, being due to chronic edema; there are also vascular dilatations, with sclerosis of the derma. (Vidal and Leloir.)

ETIOLOGY.—Women suffer more than men from the erythematotelangiectasic and acneic forms. Men only suffer from hypertrophic acne. It usually appears between 30 and 40 years. In women, rosacea develops usually at from 30 to 45 years, and increases decidedly toward the menopause, after which it may recede. It may also, however, develop at puberty.

In young women and girls acne rosacea is frequently due to chlorosis, dysmenorrhea, or sterility. In some it recurs at each conception.

Some authorities claim that, among the constitutional causes, heredity plays an important part.

Cold feet, urethral and uterine disturbances, and constipation are also recorded as causes of the disease. Exceptionally a factor in acne may be found in the mouth or teeth and be unilateral if the cause is one-sided (E. Besnier, Doyon).

Dyspepsia, neuralgia, hemicrania, working with the head inclined forward, and disease of the nasal fossæ are among the less frequent etiological factors (which affect men more than women), while high heat, overheated rooms, high wind, sea air, cold, and cold water are occasional causes, especially in men. The disease may become started in people who for several years have indulged in excessive hydrotherapeutic treatment. (Kaposi.)

Certain occupations which expose to heat, cold, winds, etc., such as those of coachman, baker, smith, fireman, glassblower, may also become primary causes of the trouble. Indiscretion in diet and alcoholic beverages are well-known factors. According to Kaposi, in wine-drinkers the nose is bright red, in beer-drinkers it is violet, while in spirit-drinkers it is soft, large, and dark blue.

PATHOLOGY.—The vascular dilatations of the face have been considered by some authorities as due to circula-

tory troubles caused by compression of the veins in the cranial foramina.

A certain paretic condition of the vascular walls may often be looked upon as a cause. (Brocq.)

The cutaneous nerves of the region affected have been found normal by E. Besnier. According to Leloir and Vidal, however, there is congestion of the deeper venous network of the skin; dilatation of the same vessels and of the perifollicular vascular network, their walls being often diminished in thickness. There is also formation of new vessels.

DIAGNOSIS.—Lupus Erythematosus.— The superficial, congestive variety shows a brighter and better defined redness; crusts or squamæ on the surface; sharper and more definite edges; greater sensitiveness to pressure; slight elevation above the surrounding surface. There are no papules, pustules, or tubercles. If any cicatrix be present, it is surely lupus erythematosus.

> Acne telangiectodes is an affection *sui generis,* and not identical with lupus follicularis disseminatus; but it is identical with the acnitis of Barthelemy, and must be distinguished from the disease known as folliculitis. It presents no sort of etiological relationship to tuberculosis, and should be separated from the tuberculomata and the tuberculides. It does not take its origin in the sebaceous glands and, therefore, does not belong to acne. Pick (Archiv f. Dermat. u. Syphilis, Bd. lxxii, H. 2, 1905).

Circumscribed Congestive Seborrhea.—In this disorder there is a limited extent of patches, shallower and more uniform redness, with crusts covering them.

Sycosis Coccogenica.—This is always an inflammatory disease of the hair-follicles and perifollicular tissues. There are numerous papules and pus-

tules, each perforated by a hair, and often capped by a small circular scale. The upper lip and chin are sites of predilection. The affection is usually painful.

Congenital adenoma sebaceum also has a special location: the nasogenial furrow, the parts around the nose, mouth, and chin. It presents a mammillated aspect, and its predilection for early youth and its normal evolution serve to establish its identity.

Eczema.—Erythematous, or pustulopapular, eczema of the face may sometimes present diagnostic difficulties. In this disease, the more or less constant, and usually intense, itching, the serous or seropurulent secretion, and the desquamation will suffice to establish the diagnosis.

Chilblains.—Changeableness of the lesions and pains are peculiar to this disorder.

Acneiform Syphilides.—Here the manner in which the elements are grouped, the long duration of their evolution, their tendency to ulceration, and consecutive cicatrix are important.

Rhinoscleroma.—In this disorder there are hard or ivory-like masses imbedded in the nose.

PROGNOSIS.—Acne rosacea does not always increase; it may remain stationary or even recede, especially in women after the menopause.

TREATMENT.— As to general treatment, it is especially necessary to pay strict attention to the good condition of the stomach and intestines, by appropriate measures and suitable diet. Purgatives are absolutely necessary from time to time; laxatives should frequently be given and constipation should be avoided (Brocq).

> In many cases, especially where the hemoglobin percentage is low or the

bowels are sluggish and irregular, the use of **Startin's mixture** is effective, the formula for which is:

℞ *Magnesii sulphatis* 30.0
   Ferri sulphatis 0.25
   Acidi sulphurici diluti 8.0
   Sodii chloridi 2.0
   Infusi gentianæ ....q.s. ad 120.0

Directions: Take a tablespoonful in half a gobletful of water one hour before each meal, using a glass tube because of the iron. If there is any indigestion this prescription may be alternated with the following:—

℞ *Papain* 8.0
   Sodium bicarbonate,
   Charcoal ....of each 16.0

Make into 50 tablets. Directions: Two tablets in a wineglassful of hot water before each meal.

J. Philip Kanoky (Amer. Jour. of Clin. Med., Aug., 1908).

Proper circulation of lower limbs should be insured by adequate clothing. Any abnormal condition of the genito-urinary tract or of the upper respiratory tract, especially the nose, should be corrected, while anything tending to cause congestion of the face, such as tight collars or stays, should carefully be avoided. Sedentary intellectual work, especially by gaslight, frequently aggravates these cases.

On the supposition that a rheumatic diathesis is a possible etiological factor, various alkalies have been recommended, especially **bicarbonate of soda** or the various **alkaline waters.**

Where the face is intermittently congested, **quinine, ergotine, belladonna, digitalis,** and **hamamelis** have been suggested. These may be combined in a mixture, with or without the **tincture** of **aconite-root.** Vasoconstrictor drugs have but little influence.

Perchloride of iron, tannin, ergot, and **tincture of hamamelis** are recommended by E. Besnier and A. Doyon.

The following preparation is extolled by Brocq:—

℞ *Quinine hydrobromide,*
   Ergotin .... of each 30 grs.
   Belladonna extract .... 6-12 grs.
   Lithium benzoate .... 30 grs.
   Excipient and glycerin ..... q. s.
Misc. For forty pills.
Sig.: Two before each of the two principal meals.

Rhubarb or **aloes** may also be added if necessary.

> Study of 12 cases of acne rosacea by the fractional method of gastric analysis. In 5 there was complete achlorhydria throughout the period of the meal and in 2 an extreme degree of hypochlorhydria. Of the remaining 5 cases, 1 showed no secretion of free hydrochloric until after 1 hour, and 2 showed a temporary high peak in the curve of acidity, with an abrupt fall to the base line. There was also a tendency to rapid emptying, and a highly mucoid resting secretion, frequently of the viscid consistency of raw eggwhite. **Dilute hydrochloric acid,** 30 minims and upward, well diluted, after meals or during meals, yielded very satisfactory results. Ryle and Barber (Lancet, Dec. 11, 1920).

The local therapeutic agents are the same as in acne vulgaris; though some irritable varieties of acne rosacea exist, it is usually necessary to act with greater energy.

Hot water and **mercurial preparations** are often of value. Mercurials are, however, much inferior to the sulphur preparations.

The following has been employed by Bazin with success:—

℞ *Mercury biniodide* .... 7½-15 grs.
   Lard .... 1 oz.—M.

Sulphur preparations, as already stated, are, however, the most useful, those commonly employed in acne being prescribed.

In cases of average intensity dermatologists frequently employ **Vleminckx's solution,** at first with 5 parts of water, then gradually making it

stronger until it is used pure. It should be left on several minutes, and followed by very hot water; it may often be left on overnight with advantage.

Green soap gives the best results in obstinate acne rosacea, alone or when used in conjunction with **sulphur, naphthol,** or **salicylic acid.** It may be used as in acne vulgaris or spread on a piece of flannel; the latter is then cut out to fit the affected region, and left on as long as possible. It should not be left on too long. When the irritation becomes too great, the application should cease and cooling preparations, such as the following, be used:

R Salicylic acid .... 7 grs.
  Zinc oxide,
  Bismuth subnitrate .. of each 30 grs
  Lycopodium .... ½ dr.
  Vaselin .... 2 drs.
  Lanolin .... 3 drs.

Ichthyol does not seem to be as efficacious in acne rosacea as in some other varieties of acne. (Brocq.)

Unna recommends daily doses of 7½ grains of **ichthyol** internally and lotions with ichthyol dissolved in water, washing with ichthyol soap. **Steam** or **sulphur-water douches** have also been used with good results.

A solution of **iodine in glycerin,** applied twice daily during three or four days, is recommended by Kaposi for the more severe forms, but it is disfiguring and not advisable for patients outside of hospital wards.

> In a series of cases of acne rosacea the author succeeded in gradually removing the eruption by means of painting with undiluted **iron chloride.** The applications were repeated every morning and evening, and resulted in a complete cure. A somewhat solid crust is apt to form at the end of four or five days, and the paintings should be omitted until this crust is cast off spontaneously. When there is much tension the surface may be covered with a clean rag that has been thickly spread with **Wilson's salve** or some other suitable ointment. In the presence of severe inflammation an **ice-bag** may be applied. As a rule, frequent interruptions are unavoidable, and the treatment is therefore likely to last about three or four months. Zeissl (Münch. med. Woch., Nu. 20, 1908).

Surgical treatment in this disease is the most efficacious. (Brocq.)

Electrolysis is another satisfactory method. A fine platinum needle is inserted alongside of the vessel, and, if possible, into it, and connected with the negative pole, while the patient holds in his hand a cylinder in communication with the positive pole. A large eschar must be avoided. (Hardaway.)

Electrolysis of each dilated sebaceous follicle with a negative platinum needle and a current of from 4 to 6 milliampères is an effective, though tedious, measure. The needle should be moved around in the follicle in order to thoroughly destroy it.

> In the early stages of acne hypertrophica, **diet,** a local spray of **sulphur lotion,** and **electrolysis** of the enlarged sebaceous glands are sufficient. But when hypertrophy occurs, with deformity and tumors of the nose, surgical measures only are satisfactory. The author prefers **thermocautery** to the knife, and considers grafting undesirable if this is used. When it is, however, **skin grafting** may hasten recovery and prevent scar contraction. Dubreuilh (Ann. de Derm. et de Syph., Nov., 1903).

The ordinary **galvanic** or **faradic currents** have been recommended by Cheadle and Piffard.

Scarification was formerly a favorite method. The best instrument is Vidal's ordinary scarificator. The skin is cut obliquely or perpendicularly to the

vessels, then slightly obliquely across these so as to form lozenges, and as near together as possible (from 1 to 1½ mm. apart), and not deep enough to penetrate entirely through the dermis, so as to avoid cicatrices.

An hour afterward the part is washed with a **corrosive sublimate solution,** 1 : 1000; then in the evening or the following day compresses dipped into an **ammonium hydrochlorate solution,** 1 : 100, or **corrosive sublimate,** 1 : 500, are applied. If too strong, warm water is to be added. If the reaction is too violent, **starch poultices, bland pomatums,** or **zinc oxide plasters** can be employed.

The treatment should be renewed in from five to eight days. Amelioration will occur in from eight to ten sessions, and marked improvement in from fifteen to twenty-five sessions.

Scarifying should be begun in the lower part of the region to be operated upon, in order not to be troubled by the blood covering the surface, according to E. Besnier and likewise A. Doyon.

In the early stage of hypertrophic acne the scarification must be made deeper, and in many cases it is essential to also **cauterize** the glands deeply.

In the advanced hypertrophic form direct **removal with the knife** is the best procedure. (Brocq.)

Hypodermic injections of alcohol have recently been recommended. **Phototherapy** has likewise given satisfactory results; both **high-frequency current** and the **X-ray** are of value in some cases.

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ACNE VACCINE. See Bac-
terial Vaccines.

ACOIN, a synthetic compound used as local anesthetic, especially in dental and ophthalmic practice. It is designated as alkyloxyphenylguanidin and occurs as a white crystalline powder, readily soluble in pure cold water to the extent of 6 per cent., and in alcohol.

A 1 : 200 aqueous solution injected under the skin causes a local anesthesia lasting about one hour. Acoin presents the drawback, however, of being quite unstable, while producing greater irritation than cocaine, and is liable to produce necrosis.

S.

ACONITE. — The preparations of aconite usually employed are obtained from the root of the *Aconitum napellus* (monkshood, wolfsbane), a conical tuber greatly resembling horse-radish. This resemblance has caused many deaths. Aconite-root is, however, brown in color, and when scraped does not emit the pungent odor peculiar to horse-radish. Again, instead of irritating the palate, as does horse-radish, aconite-root, when masticated, soon produces in the mouth a sense of warmth and tingling, soon followed by local numbness varying in duration according to the length of time the mucous membrane is exposed to the effects of the drug. Aconite owes its activity mainly to the alkaloid aconitine, of which the dried root is officially required to contain 0.5 per cent.

PREPARATIONS AND DOSE.— Aconite in substance is not employed, and the preparations made with the leaves are no longer official.

The tincture (*tinctura aconiti*, 1916 U. S. P.) is no longer stronger than the English or French tinctures. It is a 10 per cent. tincture, *i.e.*, it contains 10 Gm. of the drug in 100 c.c. *Dose,* 3 to 10 minims, every three hours. Its effects should be closely watched, especially in anemic and corpulent individuals and in those addicted to alcohol.

The extract (*extractum aconiti*, U. S. P.), ⅙ to ⅓ grain, is also official, and likewise:

The fluidextract (*fluidextractum aconiti*, U. S. P.), ½ to 1 minim.

The alkaloid aconitine (*aconitina*, U. S. P.), ¹⁄₆₀₀ grain to ¹⁄₃₀₀ grain (0.1 to 0.2 mg.), occurs in the form of colorless tabular crystals slightly soluble in water, but soluble in alcohol, ether, and chloroform.

Aconitine is a very active poison and causes the responsibility of the physician to be involved to a greater degree than any other toxic. Its activity is markedly increased when it is administered hypodermically, and the injections are very painful. These facts and the variations in strength of the various aconitines on the market have militated against its use, and it is best to utilize the other preparations, all of which owe their activity to aconitine.

MODES OF ADMINISTRATION. —Internally aconite is usually better given in small and frequently repeated doses than in large doses at longer intervals. Thus the tincture may be given in 1 minim doses every hour until the desired effect has appeared or until distinct depression of the circulation indicates cessation of the drug. Aconite should be administered well diluted. In **fever** a dram of a mixture of 10 minims of the tincture in 4 ounces of water may be given every fifteen or twenty minutes. For the relief of pain, 5 minims may be administered as the first dose, smaller ones being then given at short intervals. For **cardiac over-activity**, doses of 2 to 5 minims (0.12 to 0.30 c.c.) may be given thrice daily. When aconite is used over a long period, a gradual increase in its action is observed. Even where indicated, aconite should not be given freely with the intention of producing powerful effects, as its action in large doses is sometimes unexpectedly severe.

Aconite may be administered internally in granules, in tablets or tablet triturates such as are official in the N. F., or in solution in water (1 in 3200). Tison has used aconite nitrate dissolved in a mixture of distilled water, alcohol and glycerin, 1 minim of the solution containing ¹⁄₃₂₀₀ grain of the salt. As stated above the alkaloid should be employed with great caution, as individual intolerance of it has been repeatedly observed; a third dose of ¹⁄₁₃₀ grain (0.5 mg.) has been known to cause death (Lépine). Doses of ¹⁄₁₃₀₀ grain (0.1 mg.) may be given every two or three hours, the drug being stopped when the first signs of toxic action appear; these are, according to Gubler: prickling of the tongue, a sensation of shrinkage in the face, and loss of elasticity of the muscular openings in this region. These are followed by general numbness and chilliness. A total amount of ¹⁄₁₀₀ to ¹⁄₆₅ grain (0.66 to 1.0 mg.) in twenty-four hours may be considered the limit of safety. Dujardin-Beaumetz advised never to give aconitine unless its effects can be carefully watched.

LOCAL USE.—Aconite is used locally in neuralgia and skin affections, the tincture sometimes diluted with alcohol, or the linimentum aconiti et chloroformi of the N. F. (fluidext. aconit. 4.5, chloroform 12.5, in alcohol 100), being applied. The alkaloid is also sometimes used in a 2 per cent. ointment or in the oleatum aconitinæ, N. F. (2 per cent.), but should never be applied to abraded areas. Undiluted aconitine is absorbed through both mucous membranes and skin to a considerable extent.

Subcutaneous injections of aconitine have been given for *neuralgia,* but the pain caused and the danger from prompt toxic effects are marked disadvantages.

INCOMPATIBILITIES.—The alkaloid aconitine in solution (1 to 3200 being saturated) is incompatible with tannic acid, gallic acid, mercurials, and Lugol's solution; aconitine nitrate is precipitated as the alkaloid by alkalies. Among the physiological incompatibilities of aconite may be mentioned digitalis, atropine, strychnine, strophanthus, ammonia and alcohol.

CONTRAINDICATIONS. — By reason of its depressant action aconite is contraindicated in all cases in which prostration exists or threatens. If the respiration is embarrassed; if the heart is in asystole; if the patient is depressed, recourse must be had to tonics and stimulants. In bronchopneumonia, pneumonia after the primary stage, typhoid fever, phthisis, valvular affections of the heart, and in all cases of collapse occurring in acute infectious diseases, aconite is particularly contraindicated. In no case where the heart is weakened or degenerated should the use of aconite be considered. Old age contraindicates its use to lower the blood-pressure in nephritis.

PHYSIOLOGICAL ACTION. — Within half an hour after its administration, aconite commences to affect the general system, slowing and weakening the heart's action, lowering arterial tension, increasing the action of the skin and kidneys, and producing more or less muscular weakness in proportion to the amount taken. It causes a tingling sensation in the lips, extremities, and, perhaps, the whole body; it diminishes the rapidity and depth of the respiration, and causes disorders of

vision, vertigo, and loss of tactile sensibility and sense of pain. The effects of a therapeutic dose last three or four hours.

Aconite, when administered in sufficient dose, is a powerful depressant of the sensory nerve; some have believed that the stage of nerve paralysis is preceded by one of nerve stimulation, but Wood considers this doubtful. The drug paralyzes first the sensory end-organs, next the nerve-trunks, and finally the centers of sensation in the cord. The reflexes are correspondingly impaired. The power of voluntary movement, which continues after the cessation of the reflex functions, is finally lost, owing to the later action on the motor centers of the cord, and subsequently on the nerve-trunks. The brain is practically unaffected by aconite.

Laborde and Duquesnel state that aconite in therapeutic doses has a particular effect in modifying special sensibility in the area of the trigeminal; they believe this effect to be exerted on the bulbar receptive nuclei of the nerve. According to Cushny, the subjective sensory phenomena resulting from the use of aconitine are due to a marked primary stimulation and secondary depression of the sensory end-organs, tingling and warmth locally being followed by numbness when the drug is applied to the skin or taken by the mouth.

According to Cash and Dunstan pyraconitine, obtained from aconitine by heating to separate a molecule of acetic acid, causes no tingling of the lips or tongue. It causes slowing of the heart, partly from vagus irritation, partly from depression in function of intrinsic rhythmical and motor mechanisms. After its administration activity

of respiration is reduced (by central depression) to a degree incompatible with life. Neither muscular nor intramuscular nervous tissue is strongly influenced by pyraconitine, but the spinal cord is impaired in its reflex function, and there is a curious condition of exaggerated motility.

When aconite is applied directly to the heart, the number and force of the beats are lessened, and its action is finally arrested in diastole. It lowers the blood-pressure and pulse-rate when given internally by a direct depressant action on the heart itself, and also by stimulating the cardioinhibitory center. Laborde found, however, that the contractility of the cardiac muscle-fiber itself was not directly modified by aconitine.

Hare has called attention to the fact that the fall in pulse-rate from poisonous doses is sometimes preceded by a quickening due to a condition of weakness and abortive cardiac action. The stage of low pulse-rate is also followed by one in which the pulse is frequent and irregular. Upon the vasomotor center aconite is believed by Cash and Dunstan to have a late depressant effect. It also causes slowing of the respiration, with lengthening of the expiratory period, by depressing powerfully the respiratory center. According to some observers, small amounts of the drug produce, instead, stimulation of the respiratory function, while Cushny is of the opinion that aconitine has a primary exciting effect on most of the medullary centers—vagal, vasomotor, respiratory—as well as the spinal motor centers.

Aconite reduces the temperature both in health and in febrile conditions, probably through an action on the nervous heat-regulating mechanism, and by the circulatory depression it causes. It also increases the action of the skin, kidneys, and salivary glands. Increase of the gastrointestinal and biliary secretions is stated to have occurred. (Schroff, Rabuteau.)

MODE OF ELIMINATION.— Aconite is excreted mainly by the urinary organs, though it has also been detected in small amounts in the saliva and the bile.

ACONITE POISONING. — The symptoms following the ingestion of a poisonous dose usually show themselves after a few minutes. The characteristic tingling, prickling, and subsequent numbness already mentioned rapidly extend from the mouth and fauces to the face, thence to the body and extremities. Great prostration and muscular impotency follow. Speaking requires marked effort. The skin becomes cold and clammy, the perspiration covering the surface, and the tissues communicating to the hand an icy coldness. Muscular pains may be present in the early stages, especially in the face. There is often experienced marked epigastric pain with nausea and vomiting. Later on the nausea ceases, owing to paralysis of the stomach walls.

The heart-beats are greatly reduced in number and power. The pulse is usually irregular, compressible, slow, and so weak, at times, as hardly to be palpable; in the advanced stages, however, it becomes abnormally frequent. The breathing is labored, irregular, and shallow, the number of respirations being at first decreased, then increased. Cyanosis may appear. The temperature is lowered, sometimes considerably.

The pupils may become dilated or remain of normal size and react equally; occasionally they are contracted. According to Manquat, they undergo fre-

quent variations in size at first, then dilate. The eyes may protrude or be shrunken; therefore they afford no differential information as to the nature of the drug used.

The mind is usually clear, and the patient calm, though apprehensive of impending death. Disturbances of vision (diplopia, amblyopia) and of hearing (tinnitus, deafness), as well as vertigo, are frequently complained of. Occasionally epileptoid convulsions occur. Spasmodic purging, with rectal tenesmus and bloody stools, is occasionally present.

Aconite causes paralysis of respiration and circulation, death being due to sudden arrest of the heart in diastole.

Cases of criminal poisoning by aconite are rare, according to Magill. In the Condon case, of Springfield, Mass., the defendant purchased a two-ounce bottle of tincture of aconite, one-half of which was placed in a pint bottle of port wine and sent to the person whose life was attempted, and who drank nearly one-half of the wine. The immediate effect was dizziness, inability to move, and a peculiar creeping sensation in the muscles. The vision became obscure. Life was only saved by three hours of untiring efforts.

Case of aconite poisoning in a woman aged 45 years, a multipara, who had suffered from rheumatism, shortness of breath, and swollen feet. She drank by mistake about 3 ounces of a liniment. At once she recognized her mistake and experienced a hot tingling in the mouth, then numbness, giddiness, gastric pains, and soon thereafter followed by collapse. A druggist gave ipecacuanha wine and a strong emetic. Sickness continued, and a violent attack of clonic convulsions supervened.

The medical man called in found the patient speechless, cold, pale, skin moist, pulseless, respirations very faint and irregular, and the pupils dilated and insensitive, but no ptosis. The temperature was 96.6° F. Terrible gastric and abdominal pains and violent irritation and prickling of the skin were succeeded by numbness. Three times after attacks of clonic convulsions she appeared dead, but when they ceased the mind was clear and unaffected. As a cardiac depressant, **ipecacuanha** had been given; a **mustard emetic** was now administered to save the enfeebled heart. The head was kept low, the feet were raised, a sinapism was placed over the heart, and hot bottles and flannels were applied to the lower extremities and abdomen. **Strychnine** and **digitalis** were given hypodermically, and **brandy** was injected per rectum. **Artificial respiration** was unceasingly kept up. After an anxious six hours the breathing became stronger, an irregular, intermitting pulse could be felt at the wrist, while the body warmth slowly returned. A little coffee and brandy were swallowed and retained. The crisis passed, and she recovered. The quantity of aconite taken may be roughly estimated as sufficient to kill 6 persons. Inglis (Lancet, Jan. 21, 1911).

Death occurs in from one-half to five and half hours, the average being, according to Reichert, three and one-third hours.

The symptoms resulting from a poisonous dose of the alkaloid aconitine are the same as mentioned above, but they occur more rapidly; hypodermically administered, aconitine may cause death in less than a minute.

Treatment of Aconite Poisoning.— Death in these cases usually follows exertion by the patient. He should, therefore, be kept perfectly motionless in the recumbent position, even during emesis, his head being slightly turned and the dejections received on a towel.

An important feature of the treatment is to keep the patient as warm as possible by means of **warm blankets** and **hot-water bottles,** taking care not to place the latter against the skin. The head should also be kept warm. If the patient is seen early the **stomach-tube** should be used at once to empty the stomach. If no stomach-tube be at hand, **apomorphine,** $\frac{1}{12}$ to $\frac{1}{6}$ grain, should be administered hypodermically, or some other active **emetic,** such as **zinc sulphate,** 15 to 30 grains, be given by the mouth.

Digitalis, sulphate of strychnine, and **belladonna** are the most effective remedies, but **ether** and **ammonia** should first be employed, owing to their great diffusibility. All these remedies should be used hypodermically, the stomach being unable to perform its functions. A dram of ether, ammonia, **brandy,** or **whisky** should at once be injected, and, after a few minutes, tincture of digitalis, 15 minims; strychnine sulphate, $\frac{1}{20}$ grain; or tincture of belladonna, 10 minims, according to what the practitioner may have. **Atropine** has been recommended as the most powerful antagonist to the depressing effects of aconite on the circulation and respiration. The dosage should be regulated so as to reach the point of physiological action by frequently repeated doses. **Nitrite of amyl** may be given by inhalation, and warm, very **strong coffee** be **injected** into the rectum.

Case illustrating the physiologic antagonism between aconite and belladonna. The patient had taken by mistake half an ounce of a liniment composed of chloroform, aconite, and belladonna. This means 53.3 grains of aconite root, which represents $\frac{1}{4}$ grain of aconitine, of which $\frac{1}{16}$ grain has been known to be fatal. He also swallowed 40 minims of fluidextract of belladonna (B. P.), which is equal to 0.3 grain of the total alkaloids. This would represent, approximately, thirty times the official dose of atropine. Of chloroform he took 40 minims, about eight times the official dose. The interest in the case lies in the fact that the lethal effect of a large dose of aconite was abolished by the simultaneous action of a large dose of belladonna. Muscular weakness, numbness of the extremities, and tendency to complete collapse were the only purely aconite symptoms observed. Salivation, which is usually present in aconite poisoning, was absent, and the usually contracted pupil was overcome by the action of the atropine. Finally, the intensely depressant action of aconite on the central nervous system was counteracted by the stimulating influence of the belladonna. The obvious lesson to be drawn from the case is the great value which should be attached to hypodermic injections of **atropine** in aconite poisoning. Speirs (Brit. Med. Jour., Aug. 15, 1908).

Tannic acid is useful as an antidote. Wood recommends that it be followed by an emetic and cathartic to avoid the effects of resolution of the poison by the digestive fluids.

If the patient is seen when the stage of depression has begun through absorption of the poison, the **stomach-pump,** gently used, is alone permissible, emetics at this stage being liable to cause arrest of the heart's action. Tincture of **digitalis,** in 20-minim doses, should be injected hypodermically and repeated as required, besides the other measures indicated. **Frictions** under cover, the rubbing being directed over the heart, serve a useful purpose. **Artificial respiration** is of marked benefit and should be used persistently as long as any indication exists.

Since the strength of the tincture has been decreased (U. S. P. 1905), the cases of poisoning have been greatly

reduced, and are seldom in fact met with in literature. Hence the fact that practically all the instances recorded in these pages antedate the year of the last Pharmacopœia.

Series of cases, 6 of which were fatal, found in the literature of ten years:—

Case 1. Tincture. 7 drams. Recovery. Emetics; morphine, ½ grain; fluidextract of digitalis, 6 drops; strychnine sulphate, ¹⁄₁₆₀ grain; brandy, 1 ounce; all hypodermically. By the mouth, 2 gallons of warm water; fluidextract of digitalis, 20 drops; coffee, 11 pints; whisky, 3 pints; extract of nux vomica, ½ fluidram; port wine, ½ pint. P. F. Brick (Jour. Amer. Med. Assoc., vol. viii, p. 567, 1887).

Case 2. About 8 drops of concentrated fluidextract. Recovery. Emetics, coffee, whisky (dessertspoonful). Heat. Friction and sinapism. T. H. P. Baker (Amer. Pract. and News, vol. iv, N. S., p. 122, 1887).

Case 3. Fleming's tincture, 1½ ounces. Recovery. Emetics, brandy, ether, digitalis, ammonia carbonate. Amyl nitrite and warmth. C. C. Bradley (N. Y. Med. Record, vol. xxxii, p. 155, 1887).

Case 4. Tincture, ½ ounce. Recovery. Brandy by mouth and hypodermically. Ether. One quart of cold, black coffee. Heat and posture. S. Barnett (N. Y. Med. Record, vol. xxxii, p. 761, 1887).

Case 5. Amount not known. Patient intoxicated at the time. Symptoms of acute poisoning. Recovery. Emetics, brandy, ammonia, and digitalis by the mouth. Sixty minims of tincture of digitalis hypodermically. Heat. Clara T. Dercum (Med. and Surg. Reporter, vol. lxi, p. 1889).

Case 6. Tincture, amount not known. Child, 16 months. Marked toxic symptoms. Recovery. Brandy and fluidextract of digitalis frequently repeated in spite of vomiting. Byron F. Dawson (Med. and Surg. Reporter, vol. lxii, p. 7, 1890).

Case 7. Tincture, 2 drams. Death. Benjamin Edson (N. Y. Med. Record, vol. xxxviii, p. 365, 1890).

Cases 8, 9, and 10. Dr. Edson mentions certain other cases known of, but not treated by him, three of which died.

The amounts taken in these were from 1 to 4 drams.

Case 11. Tincture (B. P.), 1 ounce. Death in sixty-five minutes. Mustard, lavage, heat, ether, and brandy subcutaneously. L. M. Whannel (Brit. Med. Jour., vol. ii, p. 791, 1890).

Case 12. Fleming's tincture, 1 dram. Recovery. Sulphate of zinc, tincture of digitalis, 20 minims hypodermically. Whisky, 1 ounce, by the mouth, followed by calomel, 8 grains. L. M. Whannel (Brit. Med. Jour., vol. ii, p. 791, 1890).

Case 13. Fleming's tincture, 1 teaspoonful. Recovery. Mustard, spirit of ammonia comp. (B. P.), tincture of belladonna, brandy. T. F. H. Smith (Brit. Med. Jour., vol. i, p. 1109, 1893).

Case 14. Fluidextract, 4 drams. Recovery. Emetics, atropine, and brandy subcutaneously. Altenloh (N. Y. Med. Jour., vol. lxvii, p. 358, 1893).

Case 15. Tincture, 7½ drams. Recovery. Mustard, digitalis, and brandy subcutaneously; digitalis, nux vomica, and brandy by rectum; ether and ammonia by inhalation; brandy and ammonia carbonate by mouth later. G. H. Tuttle (Boston Med. and Surg. Jour., vol. xxv, p. 678, 1891).

Case 16. Mentioned by, but not seen by, Dr. Tuttle. Tincture, 5½ drams. Death. G. H. Tuttle (Boston Med. and Surg. Jour., vol. xxv, p. 678, 1891).

Case 17. Preparation not noted. Four teaspoonfuls. Recovery. Sulphate of copper, digitalis, wine by mouth; whisky by rectum; whisky, ¹⁄₂₅ grain strychnine, and digitalin, ¹⁄₅₀ grain, hypodermically. Warriner (N. Y. Med. Record, vol. xxxix, p. 521, 1891).

Case 18. Tincture, 2 drams. Recovery. Apomorphine, stomach-tube, tincture of digitalis, 25 minims; aromatic spirit of ammonia, 45 minims; brandy. Robinson (Boston Med. and Surg. Jour., p. 192, 1892).

Reported by R. W. Greenleaf (Boston Med. and Surg. Jour., July 15, 1897). [The tincture of aconite referred to is that of the old U. S. P.—Ed.]

Case of a man, aged 26, who drank about three-fourths of an ounce of the tincture of aconite. He immediately discovered his mistake, and took about a tablespoonful of ground mustard in water, but could not vomit. The writer administered **cider vinegar** about fifteen minutes after drinking the aconite. He drank about a half-pint and another half-pint out of a quart jar. In less than five minutes he was greatly relieved, and his pulse was much better. The vinegar almost immediately relieved the burning and choking sensation in his throat. His saliva, which was thick and stringy (hanging down three or four feet, at the writer's arrival, on his attempt to spit), did not change its character for at least half an hour. It gradually became normal. All the symptoms gradually subsided. C. M. Swincle (Homeo. Recorder, Oct. 15, 1908).

THERAPEUTICS.—Aconite is mainly used as a **circulatory sedative.** It lessens the blood-pressure by diminishing the force and rapidity of the heart's action, and is, therefore, indicated where a frequent and tense pulse is associated with excessive cardiac activity. It also tends to **counteract spasm** and relieve undue excitability of the nerve-centers, though its property of depressing the cutaneous sensory nerve-terminals is more marked, and is frequently availed of in neuralgic affections.

In some patients, and under some conditions of acute infection, like that of **acute bronchitis**, the reaction of the system is almost violent. The temperature of the patient rises rapidly to 104° F. (40° C.) or higher, the heart beats with greatly increased vigor and frequency, there is a full pulse of high tension, a considerable rise in blood-pressure, and an acceleration of respiratory activity. So sharp is the attack of the invading organism, and so vigorous the reaction of the system, that for the time being there seems actual danger of nature overstepping herself and creating mischief through excessive activity. It is in such cases that some external regulating influence seems advisable. In such reactions aconite is the only drug whose pharmacological provings show a true indication. A. D. Bush (N. Y. Med. Jour., Jan. 22, 1916).

Aconite causing **increased respiration**, it is indicated where, with a high pulse, there is dryness of the skin. The evaporation of sweat from the surface and the heat radiation due to the increased peripheral circulation resulting from relaxation of the cutaneous capillaries also cause a **reduction of temperature.** Aconite also possesses **diuretic** properties. Hence it appears to be endowed with all the qualities requisite in the incipient stage of uncomplicated inflammatory disorders, as an anodyne sedative.

Aconite is the most efficacious vasodilator when given systematically in full doses. Aconite thus administered at once reduces blood-pressure, produces a full and compressible pulse, and greatly increases the percentage of the elimination of urea in **interstitial nephritis.** He prefers it to all nitrites, as their vasodilating effects are too transient, the most prolonged of them, that of the erythrol tetranitrate, lasting for less than an hour, which is by no means sufficient for such a permanent morbid condition of general arterial contraction, with heightened blood-pressure, as is present in chronic interstitial nephritis. The most important action in interstitial nephritis is to increase the elimination of urea. W. Hanna Thomson (Amer. Jour. Med. Sci., Jan., 1915).

In children aconite may be given whenever the spasmodic element is clearly marked: in fever preceding attacks of **quinsy, pharyngitis,** etc.; in **asthma** and the asthmatic crises of bronchial adenopathy; in **pertussis** and other **spasmodic coughs;** in **laryngismus stridulus;** in **palpitations** associated or not with hypertrophy of the heart, and in **convulsions.**

The physiological effects enumerated afford sufficient ground for its value in the reduction of all the phenomena attending the **fever:** high temperature, dry skin, hard and frequent pulse, etc. The tincture is preferable here, as it is in all other disorders. The best effects are produced by means of small doses. One minim is first given, then another minim in one-half hour. After that, 1½ minims are given every half-hour until the febrile symptoms are reduced or until physiological symptoms of the drug appear. Aconite should always be greatly diluted.

Its antipyretic power being less than that of certain newer remedies (coaltar antipyretics), however, the latter generally (though very much less than formerly) find more favor where a marked reduction of temperature is desired, unless the additional indications for the use of aconite, such as an overactive heart, frequent pulse, or dry skin, be strongly marked. Its action in favoring perspiration may be enhanced by combination with other diaphoretics, such as the alkalies or pilocarpine.

Aconite is used in the fever attending the incipient stage of **catarrhal disorders.** It may be used as an antipyretic in continued fevers and infectious diseases,—**variola, scarlatina, erysipelas,** etc.,—but large doses are usually required, involving correspondingly great danger. It is better

used in moderate doses for general sedative and diaphoretic effects in less severe infectious fevers, such as **measles,** mild scarlatina, **rubella,** and in the group of "ephemeral" fevers. According to Tison, aconitine reduces the pain and shortens the duration of **erysipelas;** he used aconitine nitrate in doses of $\frac{1}{640}$ grain every two hours, not exceeding 10 such doses daily.

In the **reflex fever** which sometimes follows the use of the catheter it has been found very efficient by several observers.

In acute disorders of the nose, throat, and lungs the sedative effects exerted by aconite upon respiration through its influence upon the respiratory center are added to the properties previously enumerated. Hence its use in **acute coryza, pharyngitis, tonsillitis, tracheitis, bronchitis, pleurisy,** and **pneumonia.** Dujardin-Beaumetz uses aconitine when the lungs are congested, and especially in **influenza.** In all of these, 2 drops of the tincture every hour should be administered until the physiological effects—tingling and numbness of the lips and tongue—are experienced, when the remedy should be given less frequently. After the initial stage of the affections enumerated, aconite should be discontinued, especially in **pneumonia,** in which affection its administration is positively harmful as soon as the asthenic stage begins. Aconite has been used in **hemoptysis** and **epistaxis** to lower the blood-pressure and favor cessation of the hemorrhage. In the chronic disorders of the respiratory passages—including phthisis—it is more hurtful than therapeutically beneficial.

In children aconite has proven useful

in coryza, tonsillitis, spasmodic croup, asthma, whooping-cough, etc.

Aconite has been employed in all forms of **rheumatism,** as well as in gout, to relieve pain and reduce congestion. It is especially indicated when the skin is dry. It is believed to have particular value in the acute rheumatic pains due to exposure. In chronic rheumatism it may be used in the form of a 2 per cent. ointment of aconitine. Hutchinson has found tincture of aconite beneficial in **rheumatic iritis.** He gives 5 minims three times a day, in conjunction with potassium iodide and the alkalies.

Meningitis, pericarditis, and **peritonitis** are mentioned concurrently owing to the fact that their early manifestations are equally influenced by aconite. In **peritonitis** especially, its effect as an anodyne tends to prevent vomiting: an important feature. In pericarditis it increases the chances of recovery by reducing the number of pulsations, thus prolonging the resting periods between beats. It should, however, be used with caution in these conditions, in view of its somewhat variable general depressant action.

The sedative effect of aconite upon the sensory nerves and nerve-endings has led to its frequent use, internally or locally, in **neuralgia** and **neuritis.** Certain authors consider it specially effective in **neuralgia** of the trifacial nerve. In neuralgia of the intermittent type, a combination of aconite with quinine will often be found serviceable. In the form of neuralgia characterized by exacerbations during damp weather aconite is sometimes effective in small doses frequently repeated. If the painful spot does not cover much surface, application of the tincture over it with

a camel's hair pencil contributes markedly to hasten the relief. The drug may also be applied as a liniment or by inunction (see Modes of Administration). The pain of **neuritis** resulting from exposure to cold is sometimes favorably influenced by aconite. In pain due to disturbances of the central nervous structures, however, the drug has not been found of great value.

By lowering arterial tension and diminishing the number of heart-beats it may be of marked advantage in functional **cardiac disorders,** but when organic lesions are present it had better not be used. It is not infrequently employed in uncomplicated **hypertrophy,** in **nervous palpitation,** and in the **tobacco-heart,** to antagonize exaggerated action, but its effects should be closely watched lest incipient degeneration be present. The dose generally used is from 2 to 5 minims of the tincture three times daily, though some advise larger amounts.

A 2 per cent. ointment of the alkaloid aconitine has sometimes been applied to relieve pain and itching in affections such as **herpes zoster, eczema, pruritus,** etc.

> As suggested by Dr. G. W. Roberts, a solution of aconite in water is very efficient in stubborn **pruritus.** One dram (4 Gm.) of the tincture in 8 ounces (250 Gm.) of water or twice this strength may be used to "bathe" the itching area, using a soft cloth or sponge. H. T. Webster (Ellingwood's Therapeutist, Sept. 15, 1909).

Dysmenorrhea due to congestion of the pelvic organs, **metrorrhagia,** and **amenorrhea** resulting from exposure to cold have all been markedly benefited by aconite. In the **vomiting of pregnancy** aconite in moderately large doses is often found

to give relief, owing to its sedative effect upon the nervous structures involved in the reflex act.

Aconite has been used with benefit in **acute gonorrhea,** 1 minim of the tincture being given every hour (Ringer). It is also advantageous as an anodyne in **epididymitis.**

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ACROCYANOSIS. See VASCULAR SYSTEM, DISORDERS OF, under ACROPARESTHESIA.

ACROMEGALY: PIERRE MARIE'S DISEASE.—DEFINITION.—Acromegaly is a general syndrome due, in almost every instance, to tumor of the hypophysis, characterized by progressive enlargement of the osseous and other supporting tissues, and primarily and chiefly noticeable in the extremities. It was first described by Pierre Marie in 1886.

SYMPTOMATOLOGY.—The most prominent characteristic of the "acromegalic dystrophy" is, as stated above, a progressive enlargement of the extremities. Although the deformities are particularly noticeable in naturally prominent portions of the body, they also involve other regions, such as the skull, face, spinal column, and thorax, and are very marked in these regions as well.

An outline of the general appearance of the acromegalic patient—that odd, ungainly, and unharmonious creature—may prove profitable before the disease is studied in detail. His enormous, clumsy hands seem all the more massive from the fact that the forearms have retained their normal proportions. They present a "stuffed" appearance, and ter-

minate in thickened, sausage-like fingers. His broadened feet are mere paws, with toes of exaggerated size. The face is long, the forehead narrow and retreating, and the supraorbital arches enlarged; the eyes often project forward from between the thickened eyelids; the nose stretches out laterally its fleshy alæ; the lips are enormous, especially the lower, which is everted; the lower jaw is strongly prognathic; the tongue, unusually large, frequently protrudes from the mouth. This repulsive and beast-like head, bounded laterally by ears of monumental size, is bent forward and set deeply between the shoulders. Though of average stature, or above the average, the subject appears partially collapsed; the curvature of his back and the thoracic deformity contribute to his humiliation, which is further accentuated by his torpid and melancholy demeanor. From a distance his appearance is so striking that the diagnosis can be made without detailed inspection. When the deformities are fully developed, all acromegalics bear a strong resemblance, and the adage, *"ab uno disce omnes,"* is here truly applicable.

The increased bulk of the *hands* is often the first change to attract attention. The hands become broader and thicker without augmenting in length. The hypertrophy involves all the component tissues of the part,—bones, muscles, subcutaneous cellular and fatty tissues, and skin. The latter is hard, firm, free of edema, and somewhat darkened in color. The interphalangeal folds, abnormally developed, extend between what may be called wads of flesh,—the "main capitonnée." The thenar and hypothenar eminences are greatly overdeveloped, and the linear grooves of the palm are transformed into deep gutters.

The fingers are somewhat flattened from before backward, and are of equal thickness distally and proximally. The thumb measures up to 12 cm. in circumference (Lombroso), the index finger 9 cm., and the medius 10 cm. The nails remain relatively small. They become flattened, turn up at the edges, and show longitudinal striations. In exceptional cases a club-shaped deformity of the fingers, or the presence of nodosities at the interphalangeal joints, has been noted. Notwithstanding the unusual proportions of the acromegalic hand, its functions are generally preserved, complete flexion becoming impossible, however, in cases where the palm is markedly thickened. De Souza-Leite observed the "dead finger" phenomenon twice in 38 cases.

In contradistinction to this massive voluminous, or *"transverse" type,* Pierre Marie has described a second variety of deformity involving the hands. In this type they again undergo a general increase in size, but there is added a growth in length which is about proportionate to that in breadth. Being longer, the hands thus appear lighter and less clumsy than in the massive form, where the overgrowth is almost solely transverse. This *"longitudinal" type* is seen more particularly in subjects in whom the dystrophy developed at a relatively early period. We have met with it in our infantile acromegalic giants.

These deformities of the hand generally stop at the wrist, at least during the earlier stages. Later on, the hypertrophy becomes generalized, the other segments of the upper extremity—forearm and arm—being also involved.

The *feet,* like the hands, become broader and thicker, without greatly increasing in length. They present the same fleshy pads, surrounded by deep grooves. The skin is darker, but is of similar consistency. The toes, especially the great toe, reach altogether remarkable dimensions, and the nails are affected much as in the upper extremity. According to Verstraeten, the heels are always enlarged. The hypertrophic enlargement generally terminates above the leg. The knee, if early involved, is enlarged but slightly, and the foot always contrasts, by its exaggerated bulk, with the rest of the limb.

The acromegalic *facies,* besides the characteristics already noted, includes a striking prominence of the supraorbital ridges, which project to an extent corresponding to the degree of enlargement of the frontal sinuses. The eyes are lacking in expression, and appear relatively small in comparison with the capaciousness of the orbits, notwithstanding the exophthalmos occasionally observed. The eyelids are thickened either *in toto* or merely in the region of the tarsal cartilages. The temporal fossæ becoming deeper, the malar prominences appear to stand out more strongly. The nose undergoes general enlargement, and is distinctly broadened and flattened. Its alæ are heaviest inferiorly, and the septum is doubled in thickness. The lips are enlarged, particularly the lower, which is also everted. The mouth, often half open, reveals a tongue of enormous bulk. The movements of the tongue are poorly executed; the organ interferes with mastication and articulation, is frequently injured by the teeth, and sometimes shows fissures at its borders. The roof of the mouth, soft palate, faucial pillars, tonsils, uvula, and larynx all exhibit hypertrophic changes. In female subjects, the thyroid cartilage, in its hypertrophied state, recalls the "Adam's apple" normally seen in the male.
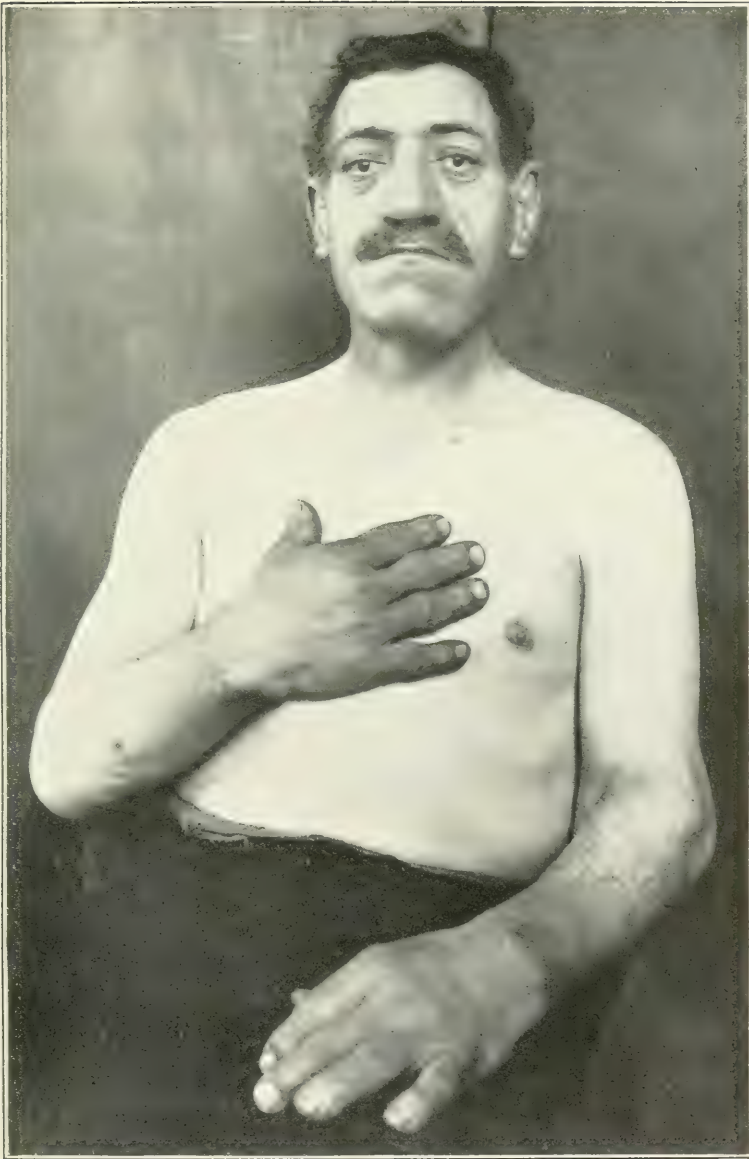
Acromegaly.   (*P. E. Launois.*)

Acromegalic Profile. (*P. E. Launois.*)

Laryngoscopic examination reveals both elongation and thickening of the vocal cords. These various changes in the organ of phonation impart to the voice a distinctive deep and at the same time metallic quality.

While the alterations in the superior maxilla are apparently not pronounced, those involving the lower jaw are sometimes extremely marked. The chin, large and massive, projects downward and forward, forming an obtuse angle with the rami of the jaw-bone. The lower teeth, which Henrot has found to be hypertrophied, are spread apart, and, owing to their forward projection, can no longer be opposed to the upper dental arch.

The profile is most characteristic, and bears witness to the extraordinary degree of prognathism sometimes attained. The description of the acromegalic facies would not be complete without a mention of the broadened ears, with their lobules of undue size.

The facial skin is dry, brownish yellow in color, and often presents warty excrescences. The hairs covering the head are individually thickened, and, taken collectively, apparently exhibit a heavier growth. The eyelashes and other short hairy appendages are also coarse and stiff.

The *bones* of the cranium proper show modifications similar to those in the facial bones. These changes will be described later, when the results obtained by radiographic examination are discussed.

In the spinal region, the vertebræ, taken as a whole, show increased volume. As a result, changes in the spinal curves are brought about, consisting, more specifically, of a cervicodorsal kyphosis, with or without lumbar lordosis and scoliosis.

The thorax becomes more capacious and undergoes alterations in shape. It becomes prominent anteriorly. Though its anteroposterior diameter is increased, it is flattened laterally. The broadened sternum tends especially to spread out above, and develops transverse ridges. The clavicles become thickened and their curves exaggerated. The ribs come mutually into contact, or even overlap, and the costal cartilages become ossified. The lower costal arches slant
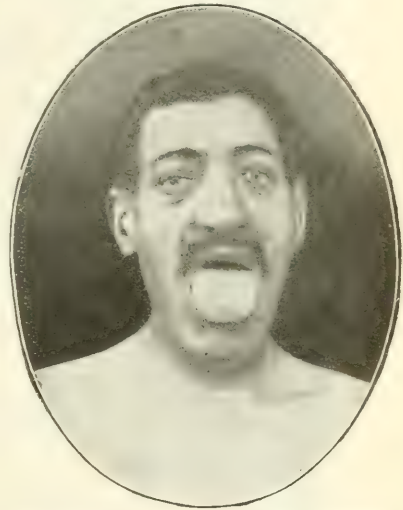
Acromegalic macroglossia. (*P. E. Launois.*)

downward, sometimes so markedly as to reach the crest of the ilium when the subject is in the sitting posture. The scapulæ are thickened, and their acromial and coracoid processes stand out in bold relief beneath the skin.

These deformities interfere in some degree with the thoracic excursions, sufficiently so, indeed, to bring about, among acromegalic subjects, a modification in the type of breathing, which becomes permanently abdominal. When they are all present in the same patient and are very pronounced, a double hump in the back may be pronounced, recalling the classic conformation of the Ital-

ian Punchinello, whom Pierre Marie considers the ancestor of acromegalics.

The dystrophy makes its first appearance at the distal ends of the extremities. The patient's attention is often attracted to the condition by the constantly increasing tightness of his gloves and footwear. In some instances the

Cervicodorsal kyphosis in a case of
acromegaly. (*Pierre Marie.*)

family or neighbors notice changes taking place in the facies. Once established, the affection progresses steadily and more or less rapidly. If the patient be a woman, she becomes aware of the progressively larger size of thimble she requires in her sewing. The male patient, on the other hand, is struck by the increasing diameter of his headgear.

From the distal portions, the changes proceed to the proximal segments of

the limbs, which, by their hypertrophy, may assume a markedly athletic aspect. Muscular power, however, almost always shows a gradual decrease; notwithstanding their bulk, the contractile power of the muscles does not bear the normal ratio to their size. A certain degree of muscular atrophy has occasionally been noted; in a case studied by Duchesneau (Thèse de Lyon, 1901) it was so pronounced as to lead this observer to suggest the advisability of differentiating an *amyotrophic form* of the disease. The muscles show no noteworthy electrical disturbances; their excitability is diminished according to Erb, exaggerated according to Verstraeten. The patellar reflexes are either normal, diminished, or lost; they are never exaggerated.

In certain *joints,* such as the knee, wrist, and elbow, there have been observed enlargement and painful crackling, recalling somewhat the phenomena noted in mild arthropathies.

The *circulatory system* presents an interesting group of alterations. Varicose veins are said to be frequent, and the heart is often hypertrophied.

[In 1895 Huchard pointed out the existence of more or less marked cardiovascular disturbances. His pupil, J. B. Fournier (Thèse de Paris, 1896), having collected 25 cases, including 12 with autopsy, was led to distinguish two varieties of cardiac hypertrophy, the one, slight and without degeneration of the muscular fibers; the other, accompanied by sclerosis and atrophy of the contractile elements. LAUNOIS AND CESBRON.]

Symptomatically these changes in the cardiac tissues find their expression in palpitations, arrhythmia, and dyspnea, and may result finally in asystole. Syncopal attacks are said to be not uncommon. Spinal deformities, when marked, may result in dilatation of the right heart.

Acromegaly in the Aged—Strabismus. (*P. E. Launois.*)

Hypertrophy of the *lymphatic vessels and glands* has also been reported.

Sensation, on the whole, does not appear to be affected. Unusual sensitiveness to cold is, however, present to a certain extent.

The various deformities that we have described arise and progress, as a rule, without giving rise to pain. In some instances, however, their development is accompanied by more or less severe painful crises, sometimes referred to the viscera, at other times to the limbs. While sometimes taking the form of a simple myalgia, they may also

striking component of the syndrome resulting from tumors of the hypophysis, and it is because it has drawn our attention to the hypophysis that the syndrome due to hypophyseal growths has brought forth such a wealth of literature as to make it at present, perhaps, the most abundantly discussed of the syndrome caused by brain tumors.

We consider acromegaly to be an integral part of the hypophyseal syndrome, and, indeed, with the exception of certain rare cases acromegaly unaccompanied by tumor of the hypophysis does not occur, while, on the other hand,
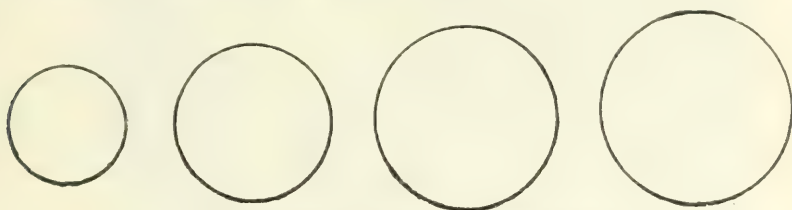
Series of thimbles used by an acromegalic woman.

develop into severe neuralgia, and are then aggravated by exposure to cold and dampness. This *painful form* of the disease (Sainton and Staté, Revue Neurologique, p. 30, 1900, and Thèse de Paris, 1900) may also assume the *rheumatoid type* when it becomes localized in a certain group of joints.

THE HYPOPHYSEAL SYNDROME.—Until recent years the natural history of acromegaly would have been covered by a description such as the above. The advances since made, however, both along clinical lines and in the pathology of the disease, owing to the use of the X-rays and to improved histological technique, have brought about modifications of our earlier ideas. Previously considered an individual affection, to which the name "Pierre Marie's disease" had properly been applied, acromegaly was found to be, in reality, only the most peculiar and

the close relationship of the disease to such tumors seems established.

The affection generally makes its appearance long before the other components of the syndrome, which may be interpreted as disturbances due to compression; on the other hand, in no case has a tumor in the region of the hypophysis been known to produce acromegaly unless developed from the hypophysis itself. Acromegaly almost certainly implies the existence of a tumor of the hypophysis. The converse is, however, not always true, every tumor of the hypophysis not necessarily resulting in acromegaly.

Clinically, tumors of the pituitary, the frequency, nature and characteristics of which we shall mention later, betray their presence by an aggregate of signs and symptoms included under the term "hypophyseal syndrome." We may divide these signs and symptoms, fol-

lowing the example of the obstetricians, into the three following groups: 1. Probable signs and symptoms of pituitary tumor. 2. Quasi-positive signs and symptoms. 3. Positive signs.

The first are those of *brain-tumor with special localization*. Through its increased size, the pituitary expands the bony fossa in which it is lodged and soon begins to project upward above it, indenting the lower surface of the cerebrum. It exerts more or less pressure on the neighboring structures, and causes a certain degree of increased intracranial tension.

The earliest symptom of it is *headache*. The pain tends to become localized anteriorly; these patients often complain of a sensation of heaviness "which impels them half unconsciously to rub their forehead and eyes, as one does ordinarily upon awakening" (Rayer). In certain cases, the pain is more definitely localized.

In some cases the progress of the disease is so nearly painless that the discovery *post mortem* of an almost complete flattening of the basal convolutions, whereas in life only trifling migraine had been recorded, becomes a matter of surprise.

Along with the headache should be mentioned *vertigo* and *vomiting* of cerebral type, which are among the usual signs of intracranial tumors.

With the symptoms are generally associated *melancholic tendencies, loss of memory,* and *mental and physical torpor*. Apathy sometimes reaches such a degree that the power of executing voluntary acts seems practically lost. It was very pronounced in the peculiar case described by Rayer: "During the morning visit, when asked to rise, he promised to put on his clothes at once, yet at 5 o'clock in the afternoon, not-withstanding repeated requests by the nurse, he was still in bed. When obliged to relinquish his room in the daytime, he would leave only to sit motionless in an armchair or to slumber in an adjoining room. The positions he assumed were those of an exhausted, flaccid, and semiunconscious individual." Convulsive movements may also be observed, sometimes confined to the face, in other instances involving the limbs.

In establishing a diagnosis of brain tumor in general, and of tumor of the hypophysis in particular, no signs should be overlooked, and we must, therefore, not forget to mention as possible symptoms *cramps, contractures*. These may be related to the coexisting hydrocephalic condition, since they disappeared, in a patient of von Hippel, upon the removal of cerebrospinal fluid through a nasal opening. The *tremor* observed by Stroebe and the *ataxia* of the lower extremities reported by Henneberg are probably to be referred to some similar cause.

Peculiar *anomalies of taste* occasionally appear, consisting of strongly expressed desires on the part of some patients to eat most unusual articles of food.

Tinnitus aurium, peculiar in that it appears only on the side upon which the patient is lying, has been noted.

Pressure may be exerted upon the sinuses adjoining the hypophysis and cause disturbances in the venous circulation, as shown by *facial edema*.

> The writer, on the basis of 4 cases observed by him, emphasizes the importance of acromegaly of the larynx, the laryngeal changes being sufficient to produce stenosis demanding tracheotomy. In one instance the latter operation alone saved the patient's life; in another case marked changes in the larynx ended in sud-

den death apparently from asphyxia. In 3 of the 4 cases the laryngeal image was not symmetrical although the laryngeal enlargement seemed so on palpation. Asthma-like attacks or dyspnea or a harsh and weak, or masculine voice in the female, may form part of the syndrome. Chevalier

for weeks at a time between 34° and 36° C. (93½° and 96⅘° F.) without the supervention of any sign of collapse.

Torpor and asthenia are, as we have stated, among the ordinary manifestations of acromegaly. Exaggeration of these symptoms, in the hypophyseal

Young acromegalic woman. In lower right-hand corner, same patient at the age of 20 soon after onset of the affection. (*P. E. Launois.*)

Jackson (Jour. Amer. Med. Assoc., Nov. 30, 1918).

Among the circulatory changes that may be produced is to be added to those already mentioned the somewhat paradoxical *acceleration of the pulse*, reported by Engel.

A no less singular manifestation is *lowering of the internal temperature*, which, in a patient of Bartels, remained

syndrome, may give the appearance of *"sleeping spells."*

True psychoses occur with extraordinary frequency in cases of tumor of the hypophysis. Schüster, who has made a special study of the psychic disturbances observed in brain tumors, believes that they are met with in almost one-half of the cases of tumor of the hypophysis. This proportion will not

seem surprising if we recall the fact that the first pathological observations on hypophyseal tumors were made in asylums for the insane. History affords a conspicuous example of this in the person of Cromwell's giant porter, a maniac with prophesying tendencies, whom it was found necessary to confine.

In the literature on the pathology of tumors of the hypophysis we often come across the words *"amaurotic insanity"* as a heading in clinical records. This accompaniment of these tumors, long overlooked, was but recently given due emphasis by Fröhlich, and particularly by Cestan and Halberstadt. The various forms of delirium, delusions of persecution, mystery, and the manic-depressive psychosis may be encountered. An interesting fact has been reported by Moutier ("Acromégalie: crises épileptiformes avec équivalents psychiques," Revue neurologique, Nov. 8, 1906) in the occurrence in an amblyopic acromegalic of rather frequent epileptiform seizures, due evidently to the cerebral tumor present. In the intervals between seizures he was subject to "absent periods," during which he would sometimes remain perfectly still, or else perform a large number of unreasoning acts of which he lost all memory after the attack had subsided.

Polyuria and *glycosuria* are often encountered in cases of tumor of the hypophysis. That the presence of sugar was not more frequently reported by the earlier observers is due to the fact that they were not in the habit of examining the urine in their cases systematically. Loeb (Deutsch. Archiv f. klin. Med., p. 449, xxxiv, 1884; Centralbl. f. innere Med., 1898) was the first to point out the frequency of melituria in disease of the hypophysis. He explained it as being due to the pressure which may indirectly be exerted by tumors of this gland on the floor of the fourth ventricle and neighboring structures.

Glycosuria of hypophyseal causation, though more or less constantly present, may show wide variations in intensity. In a patient of Finzi (Boll. della Soc. Med. di Bologna, No. 4, 1894), for instance, the sugar, after having been present in large amounts, gradually disappeared completely from the urine. In February, 1888, Strümpell (Deutsch. Archiv f. Nervenheilkunde, 1897) noted a marked glycosuria in one of his cases. In May of the same year the sugar had disappeared. It reappeared in October, then did not return, even after the ingestion of a large quantity of carbohydrates.

> Of the 176 cases of acromegaly reported so far, 35.5 per cent. included glycosuria as a symptom. Experiments were made, injecting hypophyseal extract obtained from men and horses into dogs and rabbits. In the rabbits a glycosuria varying from a slight trace to 4.2 per cent. always occurred. Borchardt (Zeit. f. klin. Med., Bd. lxvi, S. 332, 1908).

> In a case reported by the writer the glycosuria was not due to a secretion but to nerve irritation of the floor of the third ventricle by an enlarged sella. Lereboullet (Progrès Méd., Mar. 6, 1920).

> In 215 reported cases studied by the writer, 91 had thyroid lesions and glycosuria was present in 35 per cent. The pituitary disturbance seemed to precede that of the thyroid. J. M. Anders (Trans. Med. Soc. State of N. Y.; Jour. Amer. Med. Assoc., June 4, 1921).

Dallemagne, Pineles, and von Hansemann have found lesions of the pancreas at the autopsy. The first of these observers, in addition, noted the presence of small gliomatous formations in the region of the fourth ventricle.

According to Lorand the glycosuria results from disturbance in the internal secretion of the hypophysis, and is a component of one of the polyglandular syndromes, to learn the precise nature of which investigations are now being conducted.

Loeb believes it due to pressure exerted on the structures at the base of the brain, and, since, of all cerebral tumors, those developing from, or in the neighborhood of, the hypophysis are the most likely to cause glycosuria, he is of the opinion that a center regulating the metabolism of sugar exists in this region. The center discovered by Claude Bernard in the floor of the fourth ventricle would thus not be the only one of this kind; Schiff, indeed, appears to have found other such centers in the optic thalami, crura cerebri, and pons. Eckhardt produced glycosuria in rabbits by injuring the vermis of the cerebellum, and, returning to clinical and pathological records, we may recall that Lépine observed diabetes in a case of softening of the central gray nuclei, and Loeb and Naunyn in cases of cerebral hemorrhage.

According to the views of Sajous ("The Internal Secretions and the Principles of Medicine," vol. i, 1903; vol. ii, 1907; Gazette des Hôpitaux, Mar. 10, No. 29, 1907), who holds that a nervous center exists in the hypophysis, and that the several ductless glands are connected by a nervous pathway, a ready explanation is afforded. Diabetes of hypophyseal origin is the result of an irritation, a disturbance produced in the nervous center which the gland contains, in the same way that the nerve-path, in its bulbar course, is influenced by puncture of the fourth ventricle.

Whether we adopt the view of Loeb, involving pressure changes, or that of Sajous, relative to nervous irritation, however, the presence of an intermediary is further required for the production of glycosuria. According to some, this intermediary factor is the pancreas; in the opinion of Gilbert and his followers, it is the liver which, under these conditions, becomes functionally overactive; according to Sajous, it is the adrenals, to which he traced nerves from the pituitary, the adrenal secretion augmenting through increased oxidation the production of amylopsin, which, in turn, increases abnormally the conversion of the hepatic glycogen into sugar.

Rath, Oppenheim, Königshoffer, and Weil have reported polydipsia together with polyuria in the entire absence of glycosuria. Bouchard has noted peptonuria and Duchesneau phosphaturia.

Among the other disturbances of secretion, frequent and copious *sweating* should also be mentioned.

The anatomical and functional changes taking place in the *reproductive organs* in acromegalic cases were early recognized. The penis, which, as Erb correctly remarks, is also an "ἄκρον," sometimes, though not regularly, attains a greater size than normal. In the female, the clitoris may undergo corresponding hypertrophy, and the folds of skin forming its prepuce may become thickened.

This enlargement of the genital organs should by no means be taken to imply increased functional activity. Indeed, male patients usually experience a diminution of desire and potency, which may progress to complete loss of the function. In the female, the most important result is suppression of the menses, which occurs so early in the disease that in many cases it may be considered the initial event.

The primary increase in size in the genital organs soon gives way to a true atrophy. In certain cases of hypophyseal tumor which had not been accompanied by acromegaly, the penis was observed to have dwindled to the size of the little finger, the testicles to have become small and soft, and the pubic hair diminished in amount.

Pechkranz and Babinski were the first to report these changes. Roubinowitch published the interesting history of a patient, previously studied by Pierre Marie, who developed acromegaly after childbirth, and showed progressive atrophy of the organs of generation.

On the basis of published facts we may at present conclude that sexual atrophy can form part of the hypophyseal syndrome, but that it is not invariably a consequence of tumors of the hypophysis. Coming on in youth, these tumors may cause arrest of development of the genital organs; appearing later, they may cause retrogressive changes in them. The problem has not yet been solved, since it will be necessary to determine more precisely in what measure the hypophysis is capable of producing genital atrophy. The experiments of Vassale, of Caselli, and of Sacchi seem to have demonstrated that removal of the gland in young animals is without effect on their sexual development, but these animals have never survived any length of time. Moreover, a certain number of cases have been known, including those of Schmidt-Rimplex, of Götzl and Erdheim, of Babinski (Revue Neurologique, vol. viii, p. 531, 1900), of Pechkranz, and of Bartels, in which the tumor causing genital atrophy did not involve the hypophysis.

In our description of the acromegalic dystrophy we stated that the hypertrophic changes witnessed were due to an abnormal development in the various connective tissues. This overgrowth may, however, be limited to certain parts of these tissues, and in particular to the panniculus adiposus. In 1901, Fröhlich (Wiener klin. Rundschau, 1901) drew attention to a special variety of adipose overgrowth occurring in cases of tumor of the hypophysis, and attaining considerable proportions. Erdheim (Ziegler's Beiträge, Bd. 33, 1903) confirmed the association of these two conditions, and a number of cases have recently been reported. The *accumulation of fat* under these circumstances is steady and more or less rapid. It may reach an enormous extent.

With the adipose accumulations are often associated signs of increased intracranial tension, and at times, as we have remarked, mental disturbances.

We are not as yet in a position to explain the special involvement of the reserve tissues in this affection, but will have to limit ourselves to recalling the following interesting observation reported by Madelung (Langenbeck's Archiv, lxxiii, p. 1066): A girl 6 years of age, having been shot in the head, began to put on fat six months later. Her weight doubled in the space of three years and reached 42 kg. (92 pounds). Examination with the X-rays revealed the bullet in the region of the infundibulum.

Myxedema may form part of the hypophyseal syndrome. From the early observation of Norman Dalton (Lancet, No. 6, 1897) to that of Sainton and Rathery (Bull. de la Soc. Méd. des Hôp., May 8, 1908), a large number of cases have been reported which support the view that this combination may occur.

The simultaneous presence of *simple goiter* and of *Basedow's disease* has

Lipomatous Type of Fröhlich's Syndrome. (*P. E. Launois.*)

likewise been reported. Although the association of these disorders is a point in favor of the existence of a polyglandular syndrome, it would be rash at this time to attempt to define the latter precisely.

The polyglandular syndrome was clearly marked in a case observed by the writer. The right lobe of the thyroid showed a distinct enlargement of the colloid type; Addison's was shown by a brownish discoloration of the face and arms and asthenia. Bendell (Albany Med. Annals, Sept., 1915).

The writer observed a case of typical acromegaly in which an extreme degree of exophthalmos existed along with the von Graefe, Dalrymple, Stellwag and Gifford's signs of Graves's disease. Weidler (Boston Med. and Surg. Jour., Apr. 6, 1916).

Ophthalmic Disorders.—The *quasipositive signs* of the presence of a tumor of the hypophysis are found in a study of the ocular disorders, which result from the close anatomical relationship of the pituitary gland to the optic pathways. The visual disturbances long ago attracted and retained the attention of investigators. Among the earliest observations should be remembered those of Vieussens (1705), and of Rullier (1823). Ocular disturbances are also mentioned in the papers of Rayer and of Friedreich. Bernhardt has summarized them as follows: "Slow, progressive amblyopia, terminating in absolute blindness. Since the latter does not result from increased intracranial tension, but is generally due to pressure on the optic tracts, chiasm, and optic nerves, papillary edema is not generally present, primary atrophy taking place in most instances."

As for the events related more particularly to acromegaly, Pierre Marie at first recorded merely optic neuritis in

mild cases, absolute blindness in advanced cases. Pinel-Maisonneuve in France, Schültze (Berl. klin. Wochenschr., No. 38, 1889) in Germany, and, later, Boltz (Deutsche med. Wochenschr., page 685, 1892), and Packard (Amer. Jour. of the Med. Sciences, p. 660, 1892), sought to emphasize the diagnostic value of bitemporal hemianopsia, *i.e.*, loss of vision in the lateral

Acromegaly with tumor of pituitary and goiter. (*P. E. Launois.*)

halves of the two visual fields, with preservation of central vision. Since these earlier investigations, numerous observations have been collected; the present tendency, based on these, is even to establish a distinction between tumors arising in the hypophysis itself and those developing simply in the hypophyseal neighborhood. The former are not, in general, accompanied by pronounced disturbances of vision until a rather advanced stage. The morbid change in the optic nerve, however, almost always progresses, and leads finally

to complete amaurosis of one or both eyes.

The first sign afforded on systematic examination of the eyes is a diminution of visual acuity. But slightly marked at first, this generally undergoes gradual increase, absolute blindness being reached, in most instances, only after a period of ten or twelve years. Ordinarily, one eye is more seriously affected than its fellow, and shows amaurosis at an earlier period.

The condition sometimes runs a rapid course; it may disappear for a short time, then return and become definitely established. According to Oppenheim (Berliner klin. Wochenschr., No. 36, 1887, and No. 29, 1888), the histological structure of tumors of the hypophysis, which are frequently very vascular, bears a casual relation to this "oscillating vision." From the rupture of vessels with their walls in an embryonal, formative state, followed by more or less extensive hemorrhage, sudden blindness might result. Eisenlohr (Virchow's Archiv, lxviii, p. 461) reports the case of a man who, without having previously exhibited any pronounced disturbance, was suddenly seized with headache, vomiting, somnolence, and convulsive movements of the upper extremities. At the same time the pupils were dilated and fixed, and double amaurosis was present. The autopsy disclosed in the sella turcica a rounded tumor of the size of a cherry, the existence of which had not been suspected during life, and which had been the seat of an extensive hemorrhage. In like manner Bayley (Philadelphia Med. Jour., April, 1898) witnessed absolute blindness with partial oculomotor paralysis in a man of 50, who afterward showed a hemorrhagic focus in the hypophysis. With these observations may be grouped those of Bassoe (Jour. of Nervous and Mental Diseases, Sept. and Oct., 1903) and Yamaguchi. In the case of a young girl who suffered complete loss of vision in three weeks, Woolcombe (Brit. Med. Jour., June, 1896) discovered the presence of an exceedingly vascular psammoma.

Of still greater interest and importance are the alterations in the fields of vision which accompany tumors of the hypophysis, and occur with particularly remarkable frequency in acromegaly. From the standpoint of diagnosis they are of primary importance.

In 22 cases with autopsy in which changes in the visual fields had been recorded, the percentage of each form of hemianopsia was as follows: Bitemporal hemianopsia, 23 per cent.; unilateral temporal hemianopsia, 23 per cent.; homonymous hemianopsia, 9 per cent. Concentric reduction of the visual fields was recorded in 22 per cent. of the cases; an irregular contraction in 4 per cent.; in 9 per cent., but one quadrant was preserved; in 13 per cent. there was a central scotoma.

> Study of the eye symptoms in disease of the pituitary body and acromegaly based on 328 autopsies. Temporal hemianopsia is the most constant symptom; typical choked disk and slight papillitis each occurred in about 5 per cent. of the cases, simple atrophic pallor of the disks in 20 per cent., and central scotoma only in occasional cases. Paralysis of ocular muscles, generally affecting the oculomotor nerve, occurred in 10 per cent. of cases, and nystagmus in 6 per cent. W. Uhthoff (Lancet, Sept. 4, 1909).

These results will, at first sight, appear somewhat inconstant. This variability in the alterations of the visual fields is, however, to be accounted for by the fact that the visual tests were made at different stages of the affection

in the various cases. It is evident that hemianopsia and scotoma are the two most important of these disturbances.

As Déjerine pointed out, the condition present is not, strictly speaking, a true hemianopsia, since its boundaries are practically never regular in outline, and the line marking off the blind from the unaffected portions of the visual field is never exactly vertical. True hemianopsia can exist only when the lesion, situated behind the chiasm, involves the visual pathways in that part of their course which extends from the decussation to the cerebral cortex. At the chiasm itself the nerve-fibers have not yet undergone complete separation into definite bundles, and it is here that we must seek an anatomical explanation for the irregular hemianopsia which accompanies lesions of this portion of the optic pathway.

Moreover, the most varied combinations of the several ocular disturbances may occur. A central scotoma, for example, may be present at first, hemianopsia then appearing (Pontoppidan), or hemianopsia may precede and be later supplemented with marked contraction in the visual field (Strümpell). Hemianopsia and contraction are often found to coexist.

Central scotoma is of very frequent occurrence, but does not seem to possess any special value as an indication of the lesion present, since it has been observed in cases where the visual tracts appeared to be crushed by the tumor, and it is difficult to understand how, under such conditions, the maculopapillary fibers could alone be affected. Indeed, from the variations in the extent of involvement of the visual fields no conclusion can be reached with any degree of certainty as to the exact seat of the lesion. Changes in the visual fields are, however, almost constantly present; whenever examined for they have been found, and up to the present time Schönborn's case is, perhaps, the only one in which they were wanting. This observer, moreover, fails to state whether he studied the color-perception in his patient or not.

Among the changes in the eye-grounds in those suffering from tumors of the hypophysis, simple optic atrophy should receive first mention. Papillary edema, on the other hand, is of relatively rare occurrence.

The uncommon occurrence of papillary stasis may be explained by the lesions resulting from direct compression of the optic-nerve bundles. We can readily believe, with Terrien, that an intimate union takes place very early between the nerve-fibers and their sheaths in the visual tracts, and that the adhesions formed between these structures make it difficult, or even impossible, for the cerebrospinal fluid to enter the papilla.

The pupillary reflexes in cases of hypophyseal tumor also afford an interesting study, in conjunction with the disturbances of vision already mentioned. In general, it may be said that they are always altered.

In a large number of cases simple amaurosis is observed, with pupillary immobility as a consequence. Thus in a case reported by Selke (Inaug. Dissert., Königsberg, 1891), the pupils did not react either to light or distance, though the patient could still distinguish light from darkness. In a case of unusual interest, Berger observed during a period of temporary amaurosis loss of the reaction to light, while the reaction to distance was preserved. The light reflex later reappeared. In other cases, where the patients are still able to recog-

nize objects, the reflexes persist, but are less active. Yamaguchi has even witnessed very slow response to light in an eye showing normal visual acuity.

Lastly, where hemianopsia exists, the hemiopic reaction may sometimes be observed. The well-known "hemianopsic pupillary reaction," discovered by Wernicke, implies inability on the part of a visual field to bring about pupillary action in response to light falling upon it. The pupillary fibers of the optic nerve pass into the anterior corpus quadrigeminum; from here a relay of fibers starts which places them in connection with the nucleus of the pupillary sphincter, located in the central gray matter of the aqueduct of Sylvius, in the anterior portion of the common oculomotor nucleus. When these pupillary fibers are destroyed, as in cases where the optic tract has been crushed or has disappeared completely, the blind half of the visual field can no longer cause pupillary action. This reaction, then, is characteristic of an interruption in the optic fibers at a point between the chiasm and the corpora quadrigemina. The hemianopsic reaction of Wernicke is thus an integral part and almost exclusively an attribute of the syndrome resulting from disease in the hypophyseal region.

We must admit that the presence of this reaction does not appear to have been shown very often. While Josefsohn observed it very clearly, Götzl and Erdheim, in a case of hemianopsia resulting from pituitary tumor, were unable to find it. This failure and the dearth of confirmatory observations should, perhaps, be attributed to the difficulties of technique which have to be overcome in order to demonstrate the existence of this singular pupillary disturbance, which is possessed of such great clinical value for the localization of brain lesions.

Radiographic Study of the Cranium. —As for the *positive signs* of the presence of a tumor of the hypophysis, they are afforded by X-ray examination of the cranium.

No sooner had Roentgen's discovery (1895) given us the power, as Giordani expressed it, "to make of the invisible an object" than the X-rays began to be utilized in the study of the skeletal dystrophies, and of acromegaly in particular. Marinesco brought out a comparative study of the bones of the hand in acromegaly of the massive and the giant types. The data collected by Gaston and G. Brouardel were sufficiently precise to admit of the following conclusion, *viz.,* that "radiographic studies of the acromegalic hand make it possible to trace the process of central bony reabsorption and the periosteal and cartilaginous proliferation which Pierre Marie and Marinesco observed in their histological studies."

To Béclère belongs the credit of having drawn from radiographic exploration the full measure of data to be derived therefrom in the study of the hypophyseal syndrome. His first attempts were fruitless because of an entirely abnormal thickening of the cranial bones, but his later researches, especially those carried out in cases sent him by us, were productive of more accurate results. He witnessed the simultaneous occurrence of three strongly characteristic changes: (*a*) *A very irregular thickening of the cranial parietes:* the outline of the skull, instead of being rounded, is polygonal; the external and internal tables, always separated by an abnormal space, alternately recede and come together, giving a moniliform appearance on cross-section. (*b*) *Exag-*

gerated height and depth of the frontal and maxillary sinuses. (c) A more or less marked *increase* in the vertical, and especially in the anteroposterior, *dimensions of the pituitary fossa,* which, markedly altered, in most instances presents the appearance of a cup. To these primary modifications must be added *exaggeration of the postlambdoidal prominence* (Papillaut, Launois, and Roy).

increase in the size of the fossa can be plainly appreciated at its posterior wall. Schuller believes that enlargement of the bony cavity is the rule, even where the tumor is of relatively small size, and of slow, regular growth. The bony parietes may, in certain cases, undergo pressure atrophy. In cases of rapidly growing tumor they likewise disappear, being invaded by the neoplastic tissue.

Erdheim has established still nicer
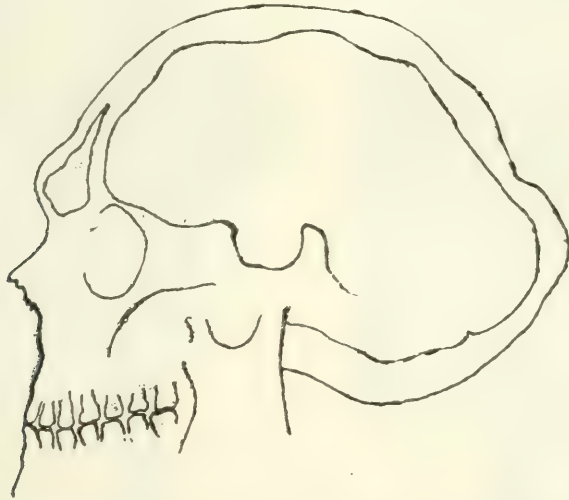
Diagram of the acromegalic skull, worked out by P. E. Launois and P. Roy, according to the X-ray findings of Béclére. Shows increased depth of frontal sinuses, irregular thickening of the cranial bones, abnormal projection of postlambdoidal eminence, and enlargement of sella turcica.

By combining the above data we were enabled to construct a diagram of the acromegalic skull, as shown in the annexed illustration.

By taking X-ray pictures from the facial aspect one can likewise learn of the changes occurring in the mandible and the degree of prognathism they may engender.

German investigators have sought to attain further precision in their radiographic studies. According to von Rutkeroski, each time the hypophysis increases in volume the sella turcica very rapidly enlarges in all dimensions; the

distinctions. According to this author, if the tumor remains limited to the sella turcica, the latter enlarges, but its aperture above does not widen. If there is a tumor of the infundibulum, the upper aperture may enlarge, but the bony fossa is little altered. Lastly, if the tumor rises above the sella turcica and bulges out over it, the fossa flares out above, presenting a broad superior opening. We may agree with Furnrohr ("Die Röntgenstrahlen im Dienste der Neurologie," Berlin, 1906) and Sternberg, that these are altogether too fine distinctions. All those who have had oc-

casion to study radiographic prints will readily understand that it is practically impossible to appreciate the trifling differences of shading upon which such distinctions must depend.

interior of the cranium, and that the borders of the sella turcica are clearly apparent. Normally a little cup-like cavity, it becomes so large, when a tumor of the hypophysis is present, that

Jean-Pierre Mazas, the giant of Montastruc (front and back views). (*Brissaud and H. Meige.*)

It is, nevertheless, a fact that the diagnosis of tumor of the hypophysis cannot today be made without the assistance of the X-rays. If, taking advantage of the improved methods introduced by Béclère, we place in the stereoscopic apparatus a reduced image on glass, we find that the body of the sphenoid is brought out in relief in the

the tips of two, three, or even more fingers can be accommodated in it.

Relationship Existing Between Acromegaly and Gigantism.—The problem concerning the relationship which gigantism bears to acromegaly is one of great interest. Our data are now sufficiently accurate to allow of its solution.

In his original description, Pierre Marie had clearly separated the two dystrophies. Numerous facts, however, were soon garnered which tended to overthrow this *dualistic view*.

The question was in reality brought to a focus by Brissaud and Henri Meige (Jour. de mèd. et de chir. pratiques, Jan. 25, 1895; Nouv. Iconog. de la Salpêtrière, 1897. Meige, Congrès de Neurol. de Grenoble, 1902, and Archives gén. de Méd., Oct., 1902, p. 410. Brissaud, Bull. de la Soc. Méd. des Hôp. de Paris, May 15, 1896) when they wrote: "The combination of acromegaly with gigantism is far from being a mere co incidence, a casual meeting between two distinct pathological states: Gigantism and acromegaly are one and the same disease. What has not been given sufficient consideration in their reciprocal relations, however, is the age at which the disease makes its first appearance. If the stage in which the bony overgrowth occurs belongs to adolescence and youth, the result is gigantism and not acromegaly. If, later on, after having belonged to youth, in which the stature is continually increasing, it encroaches upon the period of completed development, *i.e.*, upon that phase of life in which no further osteogenetic growth takes place, the result is a combination or concurrence of acromegaly with gigantism.

"Gigantism is the acromegaly of the growing period; acromegaly is the gigantism of the period of completed development; acromegalogigantism is the result of a process common to gigantism and to acromegaly, overlapping from the period of adolescence into that of maturity."

These constitute three fundamental propositions, which soon received confirmation from the labors of Woods,

Hutchinson and of one of us, published in conjunction with Pierre Roy.

As viewed by the adherents of the *unicist theory*, acromegalic gigantism is that form of gigantism in which the

Jean-Pierre Mazas, the giant of Montastruc (profile view). (*Brissaud and H. Meige.*)

characteristic loss of harmony between structure and function finds its expression, to a greater or less extent, in the usual symptoms and deformations of acromegaly, after union of the epiphyses to the diaphyses has taken place, whether this union has been prompt or delayed.

In the majority of giants almost all the stigmata of acromegaly may be recognized. Sometimes but slightly marked, the significant changes can be detected only upon careful inspection; at other times very pronounced, they attract immediate attention and are

presence of acromegaly in the person before him.

In the course of our investigations on gigantism we were led to establish a well-defined distinction between two types of giants, viz., the *infantile giant,* in whom the connecting cartilages have

Acromegalogigantism in a Chinaman. (*Matignon.*)

equally as striking as the stature of the individual afflicted with them. The disproportionate size of the hands and feet; the homely, sometimes even repulsive facial aspect; the evident sagging of the body, which is often marked, make of the subject's gigantic stature a distinction little to be envied, even in the eyes of the layman who cannot recognize the

not undergone ossification and are still able to proliferate, and the *acromegalic giant,* in whom these cartilages have become ossified and who presents bony thickenings. This distinction, having as its anatomical basis the two separate processes of cartilaginous and periosteal ossification, though a true one morphologically, does not hold good indefi-

nitely in time, *i.e.*, the infantile type, having remained pure during a certain number of years, tends to progress toward the acromegalic type, later merging into it completely. We may state, as a general conclusion, that, tumor of the hypophysis can be recognized. In 10 cases, taken from among the most recent and the most thoroughly recorded we could find, it was not once lacking. To these direct observations should be added the results obtained

Skull of the giant Constantin (profile view). (*Dufrane and P. E. Launois.*)

while all giants are not acromegalics, at least all those who are not such already are apt to become acromegalics.

Whatever be the variety of gigantism encountered, a properly conducted clinical analysis will disclose the morbid manifestations of the hypophyseal syndrome. That this is true is due to the fact that *in all giants,* whether in life by means of the X-rays, or after death on the autopsy table, the existence of a from studies of the skeletons of giants. Langer reports having found an increase in the length, breadth, and depth of the sella turcica in every case, and it is well known that in pathological states, as well as normally, the dimensions of this bony fossa in the sphenoid are those best suited for its contents.

The general conclusion warranted by all these mutually confirmatory data is

that, *whether associated with infantilism or acromegaly, gigantism always occurs in association with a tumor of the hypophysis.* This assertion cannot, of course, be given as applying to all future observations, but in view of its uniform

acromegaly with or without giantism. That the relationship between acromegaly and giantism is close is shown by the fact that a considerable percentage of acromegalics are giants and that a still larger percentage of giants develop acromegaly.

Skull of the giant Constantin (anterior view). (*Dufrane and P. E. Launois.*)

confirmation by those of the past it is, at least, very impressive.

> Hyperactivity of the anterior lobe of the pituitary coming on before the completion of epiphyseal ossification, results in giantism, that is to say, the individual is overgrown but well proportioned. After epiphyseal ossification is complete, however, hyperactivity of the hypophysis results in

Symmers (Interstate Med. Jour., Nov., 1917).

COURSE AND DURATION.— Established acromegaly is generally observed in adults, male or female. The initial dystrophic phenomena appear at the age of 18 to 25 years, *i.e.*, at the period in which, under normal conditions, growth is continued and

completed. Sometimes it is headache which leads the subject to consult a physician. Other victims, frightened at seeing their hands and feet grow larger, come to find out the reason isted, and under these conditions' the question arises in our minds whether they could not have created a disturbance in the hypophysis, as well as in the other ductless glands.
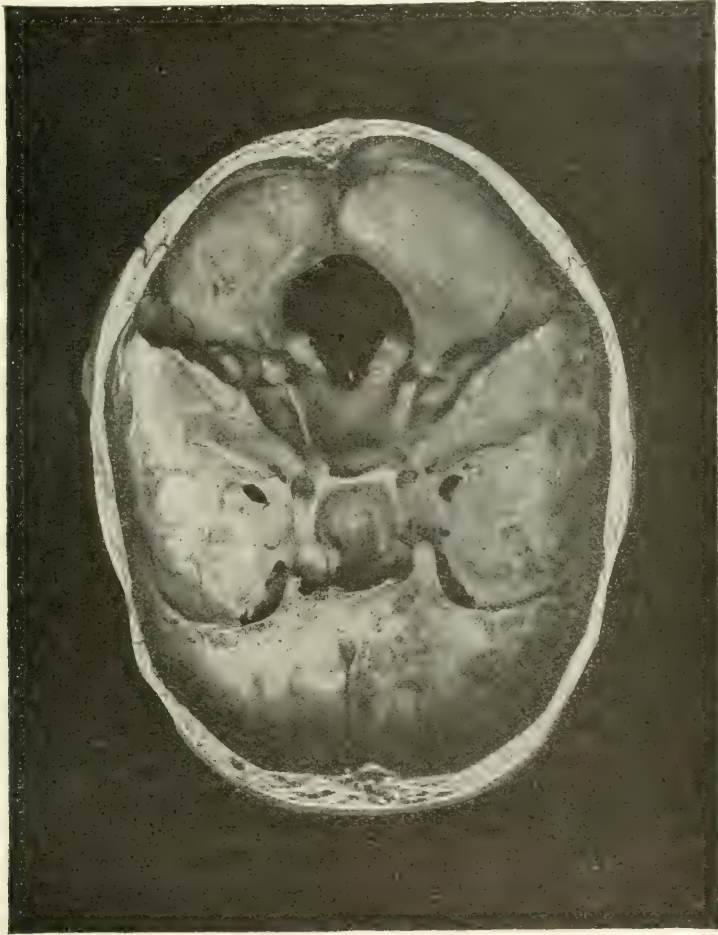
Base of cranium of the giant Constantin, showing marked enlargement of sella turcica. (*Dufrane and P. E Launois.*)

for these changes. In women the outset of the disease may be traced with some degree of probability to a period at which menstruation became irregular or ceased. We must recognize that such indications are rather vague, as is also the information obtained from the past morbid history. Sometimes infectious diseases are found to have ex-

The dystrophy seems to occur with greater frequency in women than in men. Taking the combined statistics of Souza-Leite and of Duchesneau, we find 22 men were affected as against 31 women.

While the onset of the disease is sometimes delayed (forty-nine years in a case of Schwartz), it can also be pre-

cocious, and the few cases of this kind recorded have made it possible to describe *the acromegaly of children* or *of adolescents.*

Race is without influence in the etiology. Acromegaly has been met with in all countries and among all races. Direct hereditary transmission has been observed.

Humerus of the giant Constantin. Absence of union of upper epiphysis at the age of 29 years. (*Dufrane and P. E. Launois.*)

The dystrophy follows a progressive, but extremely slow course, which can be divided into several stages. The first (stage of onset), in which the deformities begin to develop, is followed by a second (sthenic stage), in which they attain their maximum. In this stage the acromegalic woman presents a most striking appearance. The increased size of her body, accentuated by hypertrophy of the extremities; her peculiar countenance, with the lips, chin, and cheeks frequently covered with long, curly hair, and her low-pitched voice, all combine to impart a masculine appearance, which is sometimes very pronounced. In a third stage the hypophyseal syndrome asserts itself until its manifestations are more or less completely present.

The *duration* of the disease varies within wide limits (twenty to thirty years). In this connection Sternberg recognizes three forms of the affection: an ordinary form, running its course in eight to thirty years, and two rare forms, the one benign, which may last fifty years, the other malignant, destroying life in three to four years. This last form, seen only 6 times out of 210 cases, is always associated, according to Gabler, with an epithelial tumor of the hypophysis.

PROGNOSIS.—As for the termination, it is fatal. The patient at last invariably succumbs, either to the effects of a slowly developing cachexia, to intercurrent disease, or suddenly succeeding an attack of syncope or some cerebral accident.

If acromegaly be associated with infantile gigantism, the data at hand are somewhat more precise, and the onset of the disease can readily be referred to the growing period proper.

DIAGNOSIS.—The external appearances of acromegalics are so characteristic that the diagnosis is at once manifest, even from a distance. There are a few disorders, however, with which acromegaly might be confounded, and which it is necessary to differentiate.

In *myxedema,* the trunk and extremities show enlargement, which consists, however, merely of an edematous infil-

tration of the soft tissues. The thickened skin is bound down to the subjacent layers and merges into them. The round, puffy face of myxedema differs radically from the ovaloid face of the acromegalic patient, in whom, besides, prognathism and kyphosis are characteristic features.

In *Paget's disease* of the bones (*osteitis deformans*) there is increased thickness of the cranial bones and more or less marked bowing of the bones of the extremities. The thickened femora and tibia are strongly curved inward and forward, the legs are widely separated, and the trunk and neck are fixed in a position of pronounced flexion. In this affection the bones of the cranium are those involved, whereas in acromegaly the facial bones are rather affected. In the limbs the changes are limited to the diaphyses of the long bones, whereas acromegaly shows a marked predilection for the bones of the extremities and the extremities of these bones. Paget's disease, moreover, seldom appears before the age of 40, and, differently from acromegaly, attacks the various bones without order or symmetry.

Under the name of *leontiasis ossea* Virchow described a condition associated with hyperostosis of the facial and cranial bones. The lumpy appearance of the exostoses and the normal proportions of the hands and feet are sufficient to preclude all doubt as to the nature of the affection.

In *erythromelalgia* the face remains unchanged. The hypertrophic process involves only the soft tissues of the feet and hands, and is associated with an altogether peculiar cyanotic hue of the integument.

Certain cases presenting a combination of the *stigmata of rickets and of the lymphatic diathesis* might be taken for acromegalics. They exhibit clumsy hands and large feet, the lower lip is thickened and everted, and the face is somewhat puffy. But the extremities show nodal deformities of a special type, while prognathism, as well as macroglossia, are completely absent.

It is in *hypertrophic pulmonary osteoarthropathy,* the dystrophic affection seen among inveterate coughers, that confusion with acromegaly most readily arises.

Pierre Marie, who was the first to recognize and describe this form of systematized osteopathy, showed clearly, in a striking comparison he made of the two conditions, that the features wherein they differ are more numerous than their points of similarity. In both affections there is symmetrical hypertrophy of the upper and lower extremities, together with spinal curvature. But in pulmonary osteopathy, the hypertrophy, which is not uniformly distributed, is associated with distinct deformity of the parts affected. The spinal curve is altogether different from that of acromegaly, and prognathism is absent. The changes are strictly confined to the bony tissues. In the hands, the distal phalanges are clubbed, resembling drumsticks; the nails are lengthened, broadened, curved like a parrot's beak, and show cracks and longitudinal striations.

The carpal and metacarpal regions are practically normal. The wrist, however, is thickened and greatly deformed. In the feet, the distal phalanges are clubbed, the tarsus and metatarsus relatively normal, and the malleoli hypertrophied in all dimensions to such an extent that the lower part of the leg is thicker than the middle. In addition, all the long bones of the limbs are thickened, though more markedly

in the leg and forearm than in the thigh and arm. The joints are involved in these changes; their enlargement interferes with ease of motion, both active and passive. Furthermore, kyphosis is not constantly present, and when it is present is confined to the lower dorsal or lumbar regions. In the face, the superior maxillary bone is alone thickened, the mandible remaining normal.

In *syringomyelia of the pseudoacromegalic type,* the hypertrophic process is confined to the upper limbs and sometimes to a single extremity. It does not involve equally all the fingers of a hand. The parts involved are deformed and exhibit more or less marked trophic changes. The symptoms resulting from the spinal cord lesion are easily recognized.

As for certain *localized hypertrophic manifestations* (macrodactylia, macropodia, hypertrophy of a limb, or of one side of the body), described by Virchow under the name of partial acromegaly, they are congenital in most instances and bear no relationship to true acromegaly.

PATHOLOGY.—The dystrophic process in acromegaly shows a special predilection for the supporting tissues derived from the mesoderm (connective tissue, cartilage, and bone), to whatever degree of differentiation they may have attained.

The thickening of the integument is due to marked proliferation of its connective-tissue elements; the proliferation takes place in each of its various layers. Hyperplasia in the superficial stratum brings about hypertrophy of the papillæ, causing them to appear as pronounced ridges. Similar connective-tissue proliferation takes place in the walls of the sebaceous and sweat glands, in the sheaths of the hair-follicles, in the adventitia of the superficial blood-vessels, and in the nerve-sheaths. These vascular and nervous changes are not without influence on the trophic state and functions of the skin. They likewise interfere with the nutrition of the cutaneous appendages. The epidermis develops many new layers, especially in the zone of the stratum corneum; the several varieties of hair become thickened and kinked, and the nails develop longitudinal striations. Hypertrophy of the teeth has occasionally been noticed.

The connective-tissue cells of the subcutaneous panniculus adiposus in some cases become overloaded with fatty material. To this superficial adipose deposit is added, in the syndrome identified by Fröhlich, a deep-seated adipose accumulation, especially marked in the neighborhood of the peritoneal reflections.

Macroglossia is due not only to thickening of the mucous covering layer of the tongue, but also to abnormal growth of the interstitial connective tissue. The nasal, pharyngeal, laryngeal, and tracheal mucous membranes are likewise the seat of marked proliferation of the connective-tissue elements.

The alterations occurring in the fleshy portions of the muscles must also be attributed to changes of this kind. Thickening of their sheaths and of the septa dividing them into bundles brings about a marked increase in their size. Microscopically, proliferation of the nuclei and atrophy of the contractile substance are observed. The hypertrophic process extends to the tendons, of which the inserting surfaces become broader, and to the aponeurotic expansions.

Among all the changes which the supporting tissues undergo, the most characteristic, as well as the most marked, are those involving the skeleton; they

Molds of the Upper Extremities of a Case of Acromegaly. (*P. E. Launois.*)

are the result of a disturbance in the process of periosteal bone formation.

They are met with in the bones having marrow cavities, and are confined to those of the extremities and those of cancellous structure. They are also found in those membranous bones (cranial bones, inferior maxillary bone) which develop directly from the connective tissues, without being preceded by cartilage.

Whereas in adult life the periosteum ordinarily ceases to be productive except under certain experimental or traumatic conditions, of which a detailed analysis was made by Ollier, in acromegaly it is seen to proliferate and produce increased thickness of the bones by laying down new osseous layers. Pierre Marie and Marinesco (Archives de Méd. Exper. et d'Anat., p. 539, 1891), Renaut and Duchesneau, have made studies of the histological changes occurring in this abnormal type of osteogenesis. The process is described as "a slow growth of certain bones, taking place at the expense of the periosteal bone, which is reduced to thin layers, while the bony tissue of medullary origin gains in prominence, continues to develop with, so to speak, mathematical regularity, and comes to occupy a predominant position in the structure of the bone. On transverse section the entire area is occupied by red bone-marrow, containing more or less numerous fat-cells. The vessel supplying each medullary space is located exactly in its center and appears in cross-section. . . . At the periphery of the bone-marrow, in the neighborhood of the open areas corresponding to the giant Haversian spaces of cancellous bone-tissue, the rows of osteoblasts and multinuclear cells which are seen in rachitic bones are here conspicuously absent."

Summarizing the above, we may state that, whereas new layers are being added at the periphery of the bone, the central portion is undergoing actual resorption by the osteoclasts, the marrow proliferating to take its place. Recently Presbéanu (Thèse de Paris, 1909) had the opportunity, in a case of acromegaly that died as the result of a fall causing multiple fractures, to note the existence of marked demineralization of the bones; the proportion of ash, which normally ranges between 50 and 80 per cent., had been reduced to 36 per cent. These chemical changes may well account for the weakened condition of the skeleton in this disease.

In infantile giants undergoing transition into acromegaly, the changes in the bones coexist with an altogether abnormal persistence of the cartilages uniting the epiphyses of long bones to their diaphyses. In these cases the bones, while growing in thickness, also increase in length, at least for a certain period.

The articulating surfaces of the bones become broader, and the cartilaginous tissues covering them spread out without losing in depth. They may undergo some slight alterations in structure, recalling those seen in the early stages of certain arthropathies.

As for the changes occurring in the cardiovascular system, though less plainly evident than those already discussed, they are, nevertheless, well marked. The thickening of the vessel walls and cardiac hypertrophy are due to hyperplasia of the connective-tissue elements they contain. The cardiac muscular fibers may be more or less altered.

Enlargement of the heart, either simple or associated with a myocarditis, is the condition usually found in acromegaly. Sclerosis of the arteries and degenerative lesions affect-

ing the walls of the veins, with dilatation and subsequent obliteration of their lumen, are constantly present. These changes in the heart and vessels should be considered as much a part of the clinical picture as the changes in the bones, and they are probably due to the prolonged hypertension of the vessels, the result of hypersecretion of the pituitary body. Phillips (Med. Rec., Feb. 20, 1909).

The spleen and lymph-nodes sometimes appear sclerosed, so greatly has their connective-tissue network become thickened.

In a few cases a more or less generalized condition of splanchnomegaly has been reported, constituting a genuine gigantism of the viscera.

The kidneys, spleen, and pancreas had, in a few of these cases, doubled or even tripled in size.

Atrophy of certain viscera, *e.g.,* of the kidney, has been recorded in a few cases; the appearance of the renal cortex recalled that commonly found in interstitial nephritis.

In the nervous system the connective-tissue proliferation already manifested in the finer peripheral divisions then extends to the deeper branches of the nerves, which present the appearance of thick cords. The sympathetic nerve branches, and more especially the inferior cervical ganglion, have been found enlarged and sclerosed.

In a case studied by Duchesneau, the peripheral nerves showed changes due to pressure exerted on the spinal roots at the intervertebral foramina. In that of Sainton and Staté there was bony infiltration of the dura, with the formation of calcareous deposits on its inner surface, transforming it, in the dorsal and lumbar regions, into a veritable tube of lime.

The spinal cord has occasionally been found the seat of connective-tissue proliferation and localized or more or less widespread sclerosis.

In the brain, the neuroglia, which is also one of the group of supporting tissues, may proliferate more or less actively.

The Hypophysis.—Among the changes taking place in the intracranial structures, the most interesting, as well as the most important, are those involving the hypophysis.

Connected by a partially hollow stalk with the base of the brain, molded into the sella turcica, which it almost completely fills, held in position by a diaphragm of dura mater centrally perforated, and weighing on the average 0.5 gram [7½ grains] in adults, the hypophysis has long been considered an ancestral remnant, a rudimentary organ of no importance.

According to one of us, the anterior or epithelial lobe of the hypophysis is a gland of branched tubular type. The epithelial tubes or cords of which it is composed undergo anastomosis. In the spaces between them run very broad capillary blood-vessels, with very thin endothelial walls, which must be considered as the excretory ducts. The glandular cords are made up of epithelial cells loaded with granulations. In view of the different staining affinities shown by the latter, the cellular elements containing them may be divided into three classes: 1, acidophile cells, which may be eosinophiles, fuchsinophiles, or aurantiophiles; 2, basophile cells, sometimes called cyanophiles; 3, chromophobe cells. The protoplasm of these cells is always acidophile. It contains, except in the case of the young acidophilic forms and the chromophobes, zymogenic granulations, which infiltrate the epithelial elements of the glands. In addition to their acidophilic

property, the intracellular granulations possess in common the property known as siderophilia.

The primordial cell of the pituitary gland, from the morphological as well as the embryological standpoint, is a small eosinophilic cell with compact nucleus and small protoplasmic body, devoid of granulations. This cell develops along two different lines and produces either an acidophilic and siderophilic secretion or a basophilic secretion. Two distinct series of cells, therefore, exist in the hypophysis: an eosinophilic series, which becomes siderophilic, and an eosinophilic series, which becomes basophilic. The products elaborated by them having been eliminated by a semi-holocrine process, the cells of both series become chromophobic cells, which are capable of undergoing regeneration and of renewing their functional activity. The secretory product of the hypophysis is a colloid substance, giving reactions sometimes acidophilic, at other

X-ray of base of an acromegalic cranium, showing enlargement of sella turcica. (*Ch. Infroit.*)

times basophilic, and which presents analogous features with the material contained in the alveoli of the thyroid gland. We have thought it proper to introduce a summary of this cytologic

study, based on our own researches, believing that it may serve as a basis for pathological studies, the results of which thus far have been indefinite and inconstant.

Tumor of the pituitary from the giant Santos. (*Dana.*)

On the basis of facts discovered on the autopsy table, which today usually receive confirmation from radiographic studies of the skull during life, we are able to assert, as we have already shown, that hypertrophy of the hypophysis is the rule in acromegaly.

We desire to call attention to the fact that in a number of these negative cases the tumor did not originate in the hypophysis itself; that this gland was simply compressed or destroyed, and that in a few cases the histological descriptions were decidedly lacking in completeness. We must admit, nevertheless, that certain of the facts at hand leave room for doubt, which will have to be dispelled by future observations.

The gross features of tumors of the hypophysis vary. The size ranges from that of a cherry up to a hen's egg or

mandarin. The sella turcica varies similarly in its dimensions; its clinoid processes recede from one another, become blunted, and, where an infiltrating neoplasm is present, sometimes disappear entirely, together with the bony partitions they surmount.

The tumor not infrequently projects beyond the limits of the bony fossa, notwithstanding the increased size of the latter; it bulges toward and indents the lower surface of the cerebrum, and may even infiltrate it to a considerable depth.

lial origin, may be variously modified according to the type of neoplasm present, which may be sarcomatous, angiomatous, etc.

The minute structure of tumors of the hypophysis has been variously interpreted. The diversity of the descriptions given of it results chiefly, if not entirely, from the uncertainty which
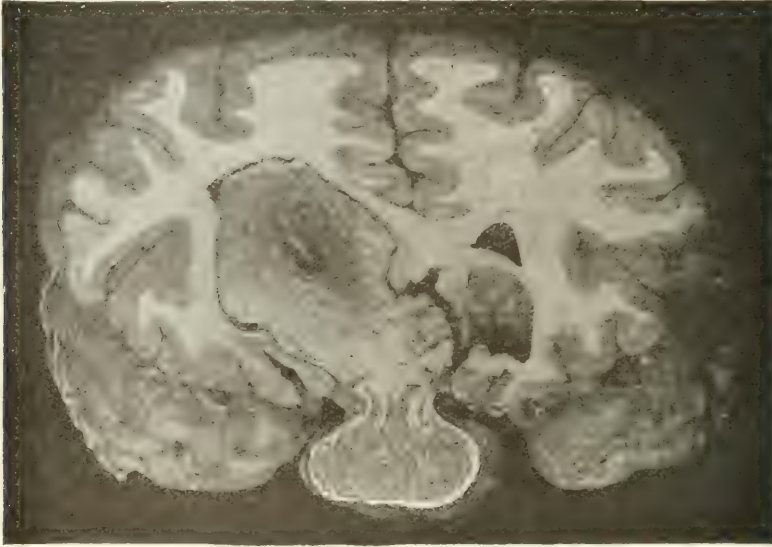
Tumor of the pituitary body extending into the right lateral ventricle.
(*P. E. Launois.*)

withstanding the increased size of the latter; it bulges toward and indents the lower surface of the cerebrum, and may even infiltrate it to a considerable depth.

In color the growth is usually grayish, sometimes yellowish; its external surface, often granular in appearance, may be dotted with small, reddish areas, representing dilated vessels or even true hemorrhagic foci. In consistency it is soft and more or less friable. On complete transverse section more or less extensive pockets of colloid material having a gelatinous appearance may be revealed.

These general features, which belong more particularly to tumors of epithe-

prevailed until within the last few years as to the normal structure of the gland.

It seems to have been shown, however, that, in a number of the cases reported, the tumor was epithelial in origin. From the 57 cases collected by him, Parona has obtained the following percentages:—

Adenosarcoma...........45 per cent.
Adenoma................26 "   "
Sarcoma................19.4 "   "
Angioma................ 3.4 "   "

These figures, together with similar statistics already published, should be taken with some reserve, and we must recognize, with Hanau, that the condition of diffuse hypertrophy of the pitui-

Primordial eosinophile cell without granulations.

*Slightly granular
cyanophile cell.*

*Granular eosinophile
cell.*

*Markedly granular
cyanophile cell containing fat.*

Siderophile cell containing fat.

*Cyanophile cell containing cyanophilic
colloid secretion.*

*Siderophile cell containing
siderophilic colloid secretion.*

Residual chromophobe cell destined to undergo regeneration.
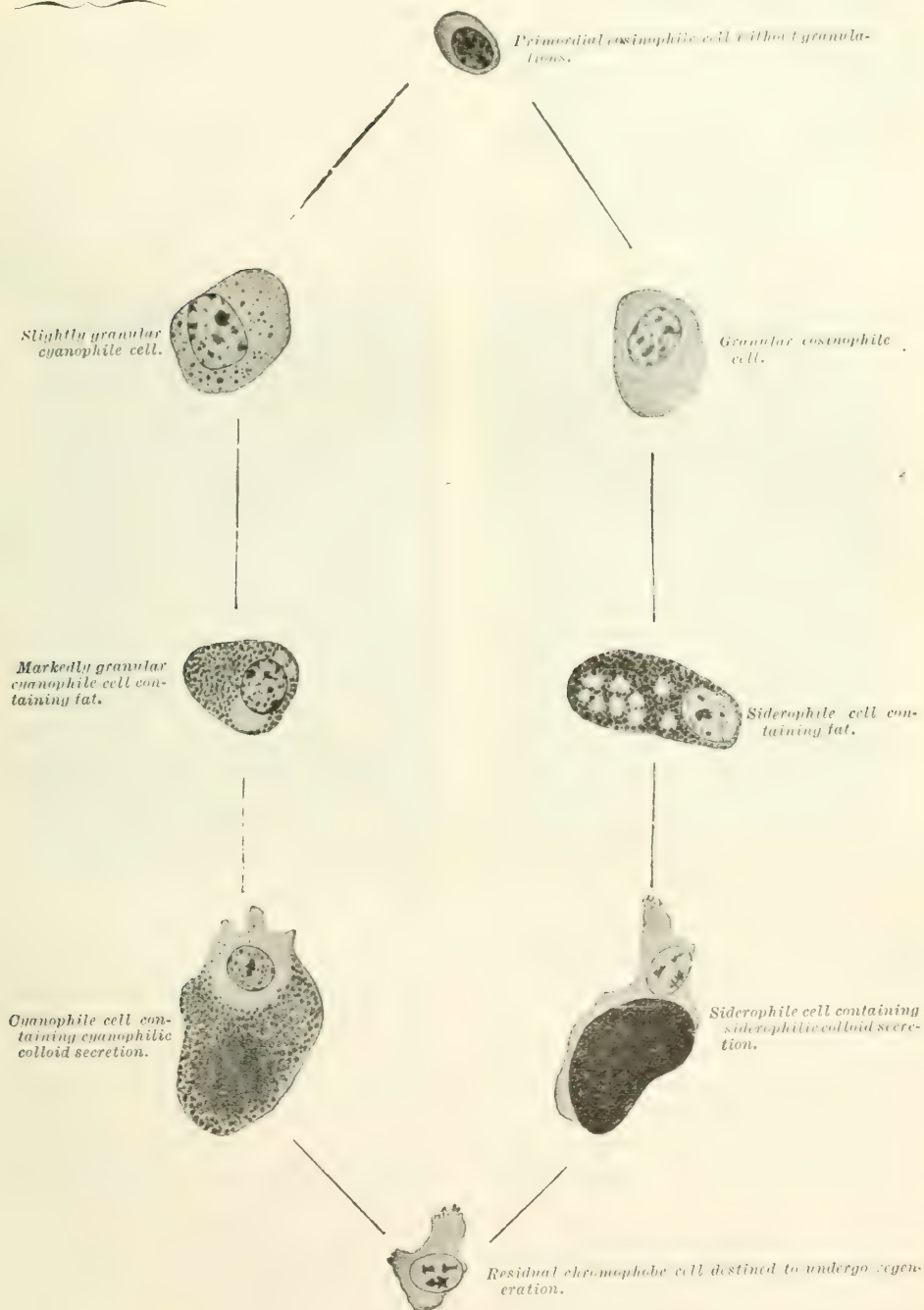
The two series of secreting cells found in the hypophysis, according to the
researches of P. E. Launois.

tary bears a marked resemblance to sarcoma.

A few of the descriptions, however, embody cytological details sufficiently definite to be of value. Among them may be mentioned the observations of Benda, who found, in three instances, that the hypertrophy was due to proliferation of the chromophile cells, *i.e.*, the functionally active elements of the gland. In a fourth case, the neoplasm was undergoing regression. Hyperplasia of the same cells has likewise been observed three times by Vassale. Lewis, in an acromegalic case which succumbed to cerebral hemorrhage soon after the onset of the dystrophy, found a pituitary which, while normal in macroscopic appearance, contained numerous large chromophilic cells.

> Study of several cases led the author to conclude that pituitary tumors of the adenoma type with cells that do not take the acid stains did not induce a tendency to acromegaly, while the latter was practically always present when the cells were acidophile. Kahlmeter (Hygeia, lxxviii, No. 10, 1916).

Enlargement of the hypophysis may also result from exaggerated growth of its connective-tissue network. Under such conditions the stage of hyperplasia of the organ, associated with expansion of the sella turcica, may be followed by a stage of sclerotic atrophy. The enlarged bony cavity does not resume its former size and appears too capacious for the gland inclosed in it. This condition was found in a case of Huchard, in which the autopsy was performed by one of us.

Instead of being generalized throughout the glandular parenchyma, the neoplastic process may be localized and appear in the form of more or less voluminous masses (partial adenomas, cysts),

reaching a variable size [Widal, Roy, and Froin (Revue de Méd., Apr. 10, 1906)].

From a general review of the facts yielded by recent investigations, the tendency has arisen to accept the conclusion that the hyperplastic condition of the hypophysis observed in acromegaly is dependent upon an increase in the number and size and an exaggerated functional activity of the chromophilic cells. This assertion, however, which to us appears premature, cannot, at present, be unreservedly accepted, for a few cases have been seen in which the hypophyseal lesion was not accompanied by any dystrophic disturbance.

In acromegalic gigantism tumors of the hypophysis are more constantly present than in simple acromegaly. We have already stated, indeed, that in the former condition they have never been found wanting. As for their histological structure, the same uncertainty prevails.

To complete this study, we shall mention the alterations which the other ductless glands may undergo in acromegaly:—

With reference to the thyroid, Hinsdale, in a series of 36 cases collected from the literature, found hypertrophy 13 times, atrophy 11 times, while in 12 cases the gland appeared to be normal.

Klebs, Massalongo, and Mossé have reported hypertrophy or regeneration of the thymus gland. Most observers have failed to inquire into the condition of the adrenals. Their study might prove fruitful, in view of the opinion of Sajous that these organs take an active part in the morbid process.

PATHOGENESIS.—According to Klebs, who had witnessed persistence of the thymus in a case of acromegaly, the affection is due to an unusual state of de-

velopment of the vascular system, and results from an angiomatous condition of the thymus. According to this view, the thymus produces endothelial elements which, swarming through the vessels, assume the rôle of formative cells in the production of fresh vessels. Thus there would result an increase in the number of vascular channels, and, in consequence, hypernutrition and aug-

states, at the age when growth ceases, *i.e.,* between the 20th and 25th years. If their functions continue after that age has been passed, acromegaly results.

Freund and Verstraeten attribute the dystrophy to a reversal in the normal order of events occurring in sexual development. "In a certain number of individuals," writes Freund, "the ordinary mode of development is disturbed.
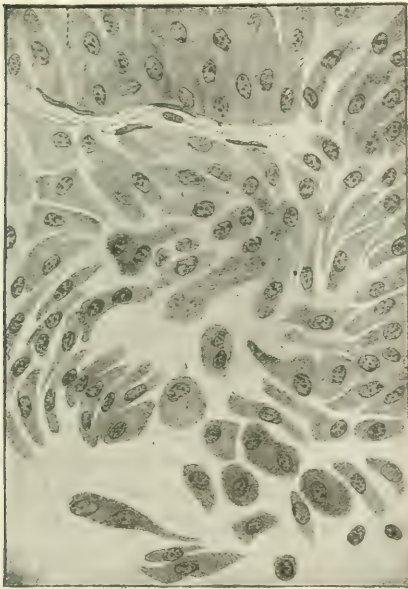
Cellular characteristics of a tumor of the pituitary. (*P. E. Launois.*

mentation in size of the terminal portions of the body, *i.e.,* of those regions of the organism in which the flow of blood slackens its speed. This power to form new vessels, however, which he attributes to the thymus, is as yet lacking in proof.

Massalongo has taken up Klebs's theory and modified it. He believes acromegaly to be due to persistence of the functions of the thymus and the hypophysis—organs which play an important part during fetal life. Normally, these glands undergo retrogression, he

Either it lags behind the norm, or else it advances beyond the norm, both in time and in space [*i.e.,* morphologically] ; the malformations which result go hand-in-hand with the disturbance in the development of puberty, and later, too, of the sexual functions." It is certain that the development of the genital apparatus is not without influence on that of the osseous system, and one of us, in a series of communications, has described the alterations produced in the bones by congenital atrophy of the testicles, of the ovaries, and

by castration before puberty. Now, the frequency with which disturbances of the genital functions are associated with acromegaly has long been noticed. But how is the influence they may exert on the growth of the skeleton to be explained? Perhaps by their suppression, diminution, or modification of a secretory product having as its purpose, as suggested by Sajous, to activate the oxidation of phosphorus-containing substances.

In short, the development of the genital functions having some influence on that of the skeleton in general, disturbances in these functions may be factors in the production of acromegaly, but they do not appear to be sufficient to bring on the dystrophy of themselves.

In the opinion of Recklinghausen and Holschewnikow, acromegaly is merely a trophoneurotic affection, dependent upon changes in the central and peripheral nervous system. Disturbances involving the vasomotor nerves would, according to this view, lead to overnutrition and hypertrophy of the extremities. There is nothing to indicate, however, that the nervous changes in this dystrophy are primary. The case on which these two observers based their opinion was one of syringomyelia.

Pierre Marie looks upon acromegaly as "a kind of systematized dystrophy, occupying in the nosological scale a position about corresponding with that of myxedema, and bearing to an organ of trophic function (the hypophysis) as yet unknown relations similar to those which unite myxedema and cachexia strumipriva to certain lesions and removal of the thyroid gland."

As this quotation shows, it was the sponsor of acromegaly himself who was the first to suspect the functional rôle of the hypophysis, "that enigmatic organ," as Van Gehuchten termed it not so many years ago.

In the preceding pages we have sufficiently dwelt upon the frequency, and even constancy, with which hypertrophy of the hypophysis, especially of epithelial origin (adenoma), is present in acromegaly. We pointed out, likewise, a condition which is daily receiving confirmation from X-ray studies, viz.: that, whatever be the mode of progression of the dystrophy, whether it take expression in its sthenic phase as the pure acromegalic type of Pierre Marie, or the lipomatous type of Fröhlich, there is present in most cases enlargement of the sella turcica, which serves to indicate hypertrophy of the pituitary body. In view of these facts, while recognizing to their full value the negative cases so far recorded, we are completely in favor of the hypophyseal theory.

Having reached this conclusion, we still have to solve two other phases of the problem, viz.: to ascertain the nature and mode of action of the disorders affecting the function of the hypophysis, and to find out whether these disorders are sufficient in themselves, or whether it is not necessary to invoke the synergistic functions of the other ductless glands as participating in the disturbance.

The experiments of physiologists, an excellent analysis of which has been given by Paulesco (L'hypophyse du cerveau, Paris, 1908), have yielded, it must be said, no definite results. Practised upon young or old animals, removal of the hypophysis produced no skeletal disorders nor acromegalic manifestations. This dearth of results is not surprising when we consider, on the one hand, the comparatively short period of survival of the experimental animals, and, on the other, the serious traumatism to

which they had been subjected in the operations. Of greater weight, as we have already emphasized, are the data afforded by the clinicopathological method. It is on the basis of these data that investigators have sought to ascertain the functions of the hypophysis, and, in particular, its trophic rôle.

Some authors, among them Tansk and Vas, and Parhon, consider acromegaly to be the result of excessive functionation on the part of the pituitary—a genuine *hyperhypophysia*. According to others, the functional rôle of the gland is to destroy substances toxic to the nervous system. The accumulation of these substances, in the presence of functional disturbance of the hypophysis, would produce, because of special predisposition, a continual state of irritation, resulting in hyperplastic changes in the bony and other supporting tissues, primarily and chiefly noticeable in the extremities. The acromegalic deformities would be an expression of functional insufficiency of the organ, or *hypohypophysia*.

The above hypotheses were those most generally accepted when Hochenegg published the results of his operations of hypophysectomy. The steady retrogression of the manifestations of acromegaly witnessed after excision of hypophyseal tumors affords an argument of the first importance in favor of the *theory of glandular hypersecretion*. Future observations will soon bring further confirmatory evidence.

The facts recorded by Hochenegg have also lent considerable support to the doctrine of the synergistic functional relationship existing between the ductless glands. In one of his cases, menstruation, which had long since been arrested, returned and was maintained at regular intervals. In 2 cases

removal of the hypophysis was followed by hypertrophy of the thyroid. We have already stated that at the autopsy of acromegalics hyperplasia of one or more ductless glands is frequently found. Furthermore, it is well known that the sexual glands exert a distinct influence on the osteogenetic activities of the connecting cartilages, and that thyroid extract is possessed of an analogous action. Caselli has expressed his belief in the identity of the functions of the hypophysis and thyroid, basing his opinion on the experimental observation that removal of the hypophysis acts on tetany parathyreopriva in the same manner as does removal of the thyroid. This functional identity, as Souques ("Acromégalie" in "Traité de Médecine" of Charcot and Bouchard, 2d ed., vol. x, p. 490) terms it, or, better, this functional analogy, would furnish an explanation for the power of mutual substitution of function exhibited by these glands under pathological conditions.

It was through surgery, practised for curative purposes, that the functions of the thyroid were revealed to us; it is through surgery that today the rôle of the hypophysis is being disclosed. It is to surgery, again, that we shall in the future be indebted for the acquisition of positive data which will enable us to solve the absorbing problem concerning the synergistic functional relationship of the ductless glands.

TREATMENT.—The treatment of acromegaly necessarily remained, for a long time, purely symptomatic, and was limited to combating the most distressing manifestations, such as pain and insomnia. Agents modifying general nutrition, such as **iodine** and **arsenic** (Campbell), were then brought into use. **Iron** in large doses and hot baths were said to have given distinct relief

in a case under the care of Brissaud. Schwartz claimed to have obtained beneficial effects from the use of **ergot**.

As a corollary to the discoveries of Brown-Séquard, opotherapic medication was resorted to. Warda and Pirie tried **thyroid** treatment without success, though Lyman Greene claimed good results with it. Napier administered powdered **ovary** to an acromegalic woman without benefit. Kuh, advocates **pituitary** substance.

> In a case of acromegaly with psychic disturbances described by the writer, all the symptoms became considerably worse while the patient took pituitary extract, whereas the administration of a **thyroid** preparation instead coincided with disappearance of the headache, dizziness, and vomiting, and an improvement in the mental state. Renewed pituitary treatment caused all these symptoms to reappear, after which they yielded again to thyroid treatment. Salomon (Presse méd., Dec. 13, 1913).

Favorsky, using Poehl's opohypophysine, noted distinct improvement in the subjective, and even the objective, symptoms. The latter observer was able to continue the administration of **hypophysine** in daily doses of 0.05 to 0.06 Gm. ($\frac{3}{4}$ to 1 grain) for fifteen months, without untoward effects. For our part, we have utilized the various animal preparations in a systematic manner and for extended periods, and have been led to the conclusion that they are entirely ineffective.

Béclère, Jaugeas and others have obtained amelioration of the pressure symptoms, including ocular phenomena by means of **X-rays**. It has also given good results after operative decompression.

The headache of acromegaly which

may become very severe is palliated by the use of **antipyrine, acetanilide,** or **acetylsalicylic acid**. Sajous obtained contraction of all soft tissues by means of **quinine hydrobromide** 5 grains (0.3 Gm.) with **ergotin** 1 grain (0.065 Gm.) **t. i. d.** and **massage** of thickened areas.

Operative Treatment. — Surgeons emboldened by the increasing safety attending their operations, were not afraid to attempt the **removal of the hypophysis**. The anatomical situation of the gland seemed to make the access to it well-nigh impossible. Nevertheless, encouraged by the results obtained by physiologists, and having gained additional information through researches on the cadaver, the operators ascertained the avenues of entrance which would permit of their reaching the pituitary gland, and on November 16, 1907, Schlosser performed the operation of removing a tumor of the hypophysis from a living person.

In theory, the hypophysis may be reached, according to Toupet, either by an intracranial or by an extracranial route. Those who favor the intracranial method advance as their chief argument the less danger of infection to which the patient is subjected, and propose either the frontal route (Krause, Kiliani) or the temporal route, already employed in their experiments by Caselli and Horsley.

At the present writing (1918) the chief indication for operation is to relieve the pressure of the growth on surrounding important structures. Hence the term "decompression operation" now extensively used. The tumor may be partially removed, or space in neighboring structures of little importance may be provided to

accommodate it if it cannot be removed.

Special precautions are necessary when an operation is to be resorted to.

especially thin in most instances. The tumor may itself alter greatly the shape of the sella and erode its walls sufficiently to penetrate it. A
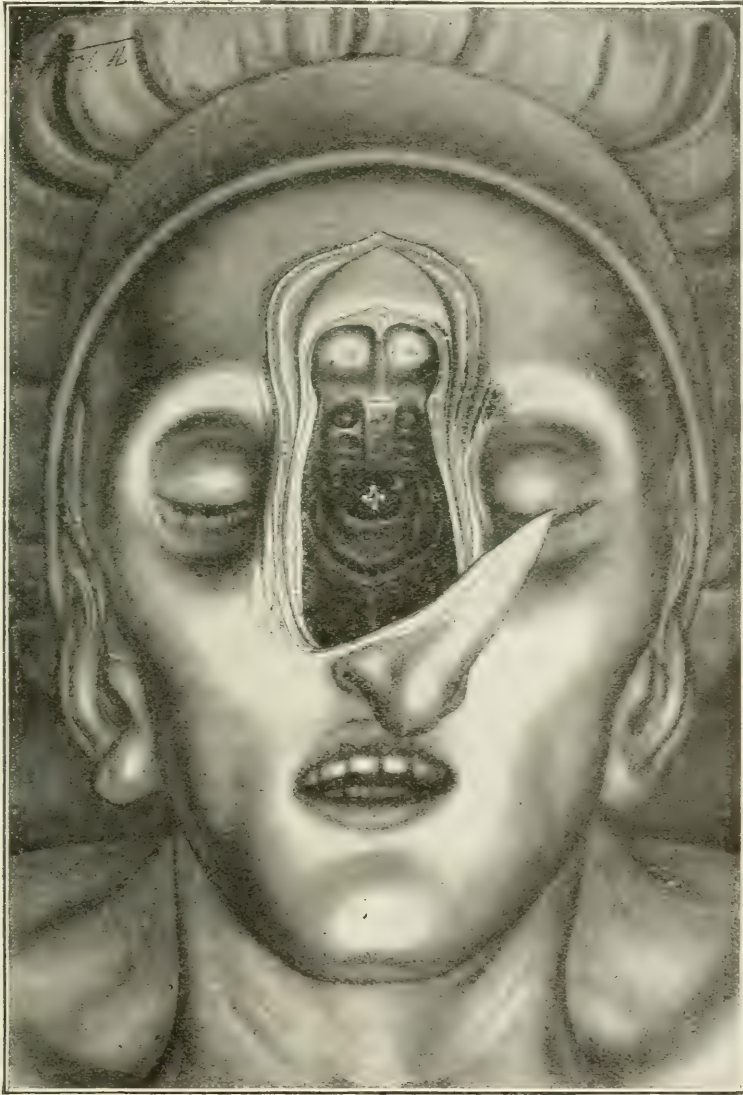
The pituitary, marked with a white cross, can be seen in its dorsal sheath. (*R. Proust.*)

Both the sphenoidal cells and the sella turcica vary greatly in size, depth, shape and thickness, the posterior of the sphenoidal sinus being

radiograph will furnish an outline of the sella and afford a pretty correct estimate of the size and location of the growth.

A trained brain surgeon should be entrusted with the operation. Some prefer general anesthesia, others local anesthesia, a strong solution of cocain (20 per cent. solution) with adrenalin being used.

In the United States two methods have proven fairly satisfactory. The Hirsch-Cushing submucous nasal method and the fronto-orbital method of Frazier.

In the **Hirsch-Cushing operation** intra-tracheal anesthesia is employed. The upper lip is raised and a short incision made down to the anterior nasal spine of the superior maxilla, the soft parts scraped back until the cartilaginous septum is exposed, and the septal membrane then separated on each side as in submucous resection. Upon insertion of a retractor 1.8 cm. in breadth and 6 cm. in length, to separate the freed layers of mucous membrane, most of the vomer, the lower edge of the median plate of the ethmoid, and a small strip of the cartilage are removed. A series of dilating plugs, up to a diameter of 1.8 cm. are now introduced to flatten the turbinates slightly, the retractors then withdrawn, and a self-holding, bivalve speculum, with blades about 7 cm. long, inserted. The sphenoidal sinuses having been identified, their anterior and lower walls are chipped away with long-handled nasal rongeurs, the lining mucosa of the sphenoid cells removed, and the floor of the pituitary fossa, forming a protrusion into the cells, also chipped away. With a knife-hook a crossed incision is finally made in the dura covering the pituitary or growth, and the latter appropriately dealt with. Termination of the operation consists merely in checking bleeding completely, with-

drawing the speculum, and closing the lip incision by means of two or three catgut sutures, without drainage. The 2 layers of septal membrane, as a rule untorn, fall together, and the entire procedure is thus conducted without actually entering the nasal passages.

The mode of procedure as regards the exposed pituitary area depends upon the lesion discovered. A mere growth under the sella proper arising perhaps from a pituitary rest may be removed. If, as is usually the case, the tumor is located higher up and large, even composed of pituitary tissue, the sellar decompression described may suffice to restore vision by relieving the pressure on the optic nerves. A later operation may become necessary, particularly if the nature of the growth is in doubt. When a greatly enlarged sella is filled with a large pituitary growth, the portion of the latter resting on the sella may be scooped out with but little bleeding. An intrapituitary cyst should be evacuated.

> Out of 95 operated cases the writer had in 37 subtemporal decompression 2 fatalities, 8 subtemporal explorations without mortality, 6 subfrontal explorations with 1 death, 16 transphenoidal decompressions with 3 deaths, and 58 transphenoidal extirpations, with 4 deaths. The total operative mortality was thus 8 per cent. and the case mortality, 10.5 per cent. In the last 33 transphenoidal operations there was but 1 death,—a mortality of only 3 per cent. C. Cushing (Jour. Amer. Med. Assoc., Oct. 31, 1914).

In the **Hirsch method** the middle turbinates are usually removed as a preliminary measure some days before the main operation. At the latter, performed under local anesthesia,

the initial incision is made through the mucous membrane over the nasal septum, on one or the other side. Special precautions are taken to insure asepsis. The exposure of the pituitary is transphenoidal, as in Cushing's procedure. Of 26 cases thus dealt with, 4 succumbed as a result of the operation.

The writer employs **Hirsch's method** with a slight modification; he detaches one of the mucous membranes in order to render the spheno-hypophyseal cavity accessible by a nasal fossa. This he deems very important when treating neoplasms originating from the sella turcica which become extrasellar, and penetrate into the cerebral cavity and consequently incapable of total extirpation. The modification is also useful where intrasellar growths have a tendency to recur. By insuring easy access to the sphenoidal cavities and keeping in contact with the sella turcica, it facilitates the subsequent use of radiotherapy. His 7 cases promptly healed by first intention. E. V. Segura (Rev. Asoc. med. Argent., xxvii, 984, 1917).

Although recognizing the value of Cushing's method and its excellent results, the writer contends that it entails danger of meningitis owing to the fact that the sphenoidal ostia open into the nose. He deems Frazier's fronto-orbital method (see below) more suitable than the submucous procedure in most cases. While Frazier had no mortality in 4 cases, Cushing's series of 16 cases had 1 death. Cope (Lancet, Mar. 18, 1916).

In **Frazier's operation,** or fronto-orbital method, the relation of the frontal sinuses to the supra-orbital margin is first ascertained by transillumination. An osteoplastic flap is then formed in the frontal region, the incision starting at the external angular process, coursing through the eye-brow line to the root of the nose, ascending to within the hair line, turning outward again, and returning to the temporal region on a level with the beginning of the incision. In forming the bone flap the outer portion of the supra-orbital ridge is removed as a wedge-shaped piece. The periosteum is then freed from the roof of the orbit, the roof removed with rongeurs back to the optic foramen, and if necessary, a small opening made in the dura to permit cerebrospinal fluid to escape and thus allow greater displacement of the frontal lobe. The orbital contents are drawn downward and outward, with flat retractors, the frontal lobe with its dural covering raised, and the dura then incised horizontally about a centimeter above the base of the skull sufficiently to admit a retractor and expose the contents of the sella.

The advantages claimed for the fronto-orbital route are, that it provides an aseptic route, that it allows each step of the operation to be performed under direct vision, and that since the primary enlargement of pituitary tumors is towards the brain, the organ is thus an easier object for attack than it is from the infrasellar exposure.

For the removal of cysts **Kanavel's operation** is advantageous. The incision is made in the crease of the skin immediately under the nares and alæ of the nose. The nasal spine is then cut and the mucous membrane carefully raised from the floor of the nose and off of the septum, back to the sphenoid bone and off from the front of the latter. The pituitary is then exposed through the sphenoid as in Cushing's operation. In the first of Kanavel's cases the cyst found was

thoroughly curetted, with the result of bringing the existing typical Froelich syndrome to a standstill and relieving the marked signs of intracranial pressure. Dried pituitary gland was fed for over 3 years. Six

ous titles such as epithelial tumors of the infundibulum, papilloma of the choroid plexus, cystic endothelioma of the pia, adenoma, adenosarcoma, dermoids, etc. The epithelial inclusions forming the starting-point of such tumors reach the pituitary from
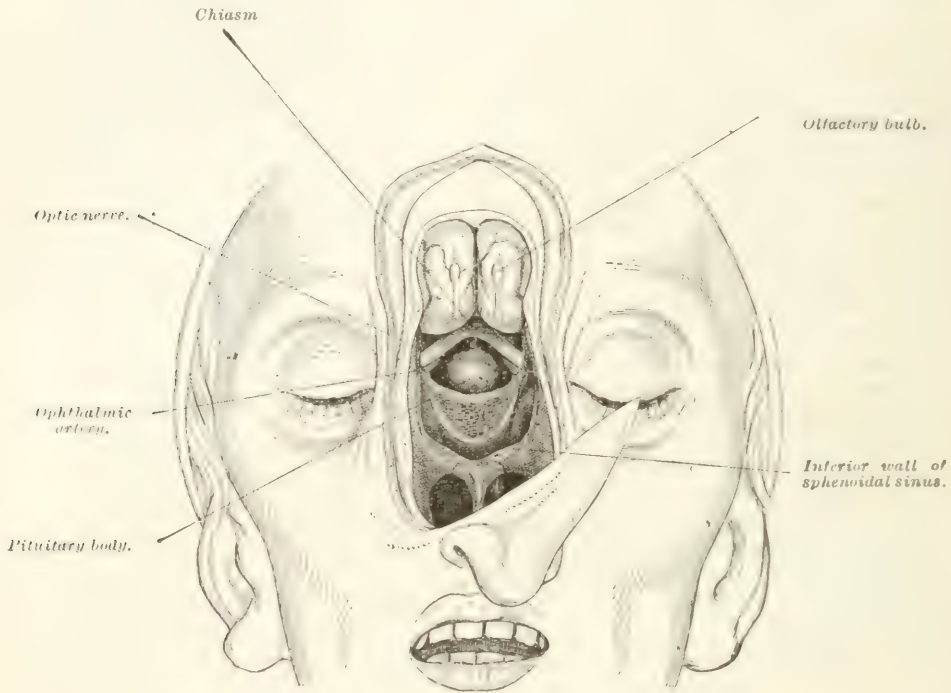
Relations of pituitary body, as exhibited by removal of the bony floor of anterior cerebral fossa. (*Proust*)

years after the operation the patient was still living and well. The second case succumbed to meningitis after the operation, while the third was operated upon on 3 successive occasions for pressure relief, with ultimate recovery. Three years after operation there had been no recurrence of symptoms.

These cysts actually arise through inclusion of buccal epithelium in the hypophyseal region, the remains of Rathke's pouch, *e.g.*, persisting near the infundibulum and later proliferating to form cystic or adamantine tumors, hitherto reported under vari-

the craniopharyngeal duct, which in the embryo forms a passage from pharynx to brain cavity traversing the sphenoid bone. Kanavel (Surg., Gynec. and Obstet., Jan., 1918).

As previously stated, **X-ray** treatment is often resorted to advantageously by Cushing after operations, when the growth tends to enlarge rapidly or to recur. The exposures are made through the nares and over the temple on alternate days.

Different measures should be adopted under different circumstances: (1) comparatively small tumors in the sella turcica covered with a tent of dura

mater can be removed completely by the nasal route; (2) growths growing endocranially, but filling the sella turcica, can be removed in part to relieve the pressure symptoms, though not the acromegaly; (3) endocranial growths, removal of which can only prove harmful. Hochenegg (Deut. Zeit. f. Chir., Bd. c, S. 317, 1909).

Confirmation of Paulesco's observation that simple division of the stalk of the pituitary is as fatal a procedure as removal of the latter organ also, and also of the view that the latter procedure in animals is invariably followed by death within a few days. This fatal result is evidently due to removal of anterior or epithelial lobe, since removal of the posterior or neural lobe is followed by no characteristic symptom. Cushing and Redford (Johns Hopkins Hosp. Bull., April, 1909).

P. E. Launois
and
M. H. Cesbron,
Paris.

ACTINOMYCOSIS.—DEFINITION.—A parasitic, infectious, and inoculable disease due to the development of the actinomyces, or ray fungus. First described in 1877 in cattle by Böllinger and in man by James Israel; it can no longer be considered a rare disease. From its frequent development in the lungs it has often been confused with tuberculosis.

SYMPTOMS.—The symptoms vary according to the locality of the disease. The affection is chronic and exceptionally rapid. The granulation tissue is abundant and the mass resembles a tumor. Previous to suppuration it is quite firm, and, if progressing rapidly, is surrounded by diffuse edema. Pain and tenderness hardly ever exist. When suppuration occurs the mass increases rapidly in size.

Actinomycosis may develop in almost any part of the body, but Poncet and Bérard showed, after an investigation of 500 reported cases, that the sites of predilection were relatively as follows: Head and neck, 55 per cent.; thorax and lungs, 20 per cent.; abdomen, 20 per cent.; other parts, 5 per cent. In France the face and neck were affected in 85 per cent. of the 66 cases reported.

Actinomycosis should always be considered in the diagnosis in the case of any newly formed subacute or chronic swelling in the region of the mouth, face, neck, thorax, or right side of the abdomen. Pus from every abscess should be examined as a routine practice. In any subacute or chronic lesion, the discharge needs to be examined repeatedly. Peribuccal infections comprise the majority of the cases. Cope (Brit. Jour. of Surg., July, 1915).

1. Cutaneous Surface.—Usually, a lesion of the skin is secondary to the evolution of an underlying actinomycotic tumor, which, by its growth, bursts through the skin. A sanguineous or purulent liquid, containing the characteristic grains, issues from the ulcerations so formed. The grains are small, opaque, yellowish-white, or yellowish masses about as large as a pinhead, which are composed of smaller grains, measuring about $\frac{1}{10}$ mm. These smaller grains are formed by a central mass, of interwoven or straight fibers, whence extend toward the periphery spoke-like prolongations, with club-like terminations. Rarely the affection may develop primarily on the fingers, hand, nose, or face. It forms a small, round, ligneous mass, which may soften in a few weeks, burst through the skin, and give a granulous and varied pus, containing actinomycotic granulations. The border of the granulation is uneven, violet-hued, and undermined. Around the original mass there arise secondary masses; so that the entire lesion forms a violet-red, in-

durated patch, deeply adherent, and somewhat resembling scrofuloderma.

In cutaneous actinomycosis the lymphatic ganglia are usually not enlarged. Pain is, in some cases, intense; in other cases it is awakened only by pressure. The pathognomonic spots, which are more or less deep in color, according as the general color of the lesion is more or less pronounced. If the general color is pale, the spots are bluish red or violet; if the tint of the mass is deeper, the spots present a blackish or slate color. These spots vary in size from that of a pea to that of a pin's head. They appear to correspond to the points at which the wall of the abscess is thinnest, and it is here alone that fistulæ form.

In some instances, as in the case reported by Pringle and illustrated in the annexed colored plate, the lesions may assume the appearance of large sarcomatous-looking growths, ulcerating at various points, situated upon hard, brawny, and deeply undermined skin and from the ulcerative points of which pus exudes, mixed with characteristic yellow granules, actinomycosis.

2. Alimentary Canal.—*Teeth.*—The fungus has been found in carious teeth (Israel), often side by side with leptothrix (Senn), or almost pure culture with no manifestation of disease except chronic periodontitis (Partsch). Carious teeth have increasingly been shown to act as etiological factor of the affection.

Tongue and Tonsils.—In man three cases of this affection have been found on the tongue, one of which was of primary development; the other two are believed to have found origin in a carious tooth. The tonsils may also be affected and be the seat of white projections resembling masses of moss, which seemed to grow in the crypts. The

pharyngeal wall also shows these white masses, as a rule.

Lingual actinomycosis in cattle appears as a nodular tumor, with prolongations into the parenchyma, of ligneous hardness.

Jaws.—The lower jaw is the most frequently affected. At first the disease resembles periosteal sarcoma, until the loose tissues of the neck are reached, when it often rapidly extends downward along the subcutaneous connective tissues and intermuscular septa. According to Poncet, an early sign of actinomycosis in this location, in some cases, is a marked difficulty in opening the mouth, long before the presence of the disease can be determined microscopically.

The upper jaw is rarely primarily affected. It then tends to attack rapidly the adjacent parts, and even the base of the skull and brain.

> A primary actinomycosis infection of all salivary glands can take place. The disease in the early stage has a definite clinical as well as pathologic picture. In a relatively short time the writer observed 9 primary cases. Eight of these were very early cases of primary actinomycosis of the salivary glands. Altogether he reports 31 cases, 7 of which originated from the submaxillary gland. The infection entered positively by the duct route in some of the cases and probably in the others also, the patient chewing a stem of grain bearing the actinomycotic organism. Three different stages are observed: a diffuse inflammatory process, a localized abscess, and a spreading abscess within the gland, eventually forming new abscesses and finally breaking through with the formation of fistulæ, either external or internal. G. Soderlund (Nord. med. Ark., xlvi, No. 4, 1914).

3. Intestinal Canal.—The disease begins with a sharp, lancinating pain in

Case of Actinomycosis Extensively Involving the Skin. (*Pringle.*)
Transactions of the Royal Medico-Chirurgical Society.

the abdomen and follows the course of chronic peritonitis. Swellings forming abscesses are found on the anterior abdominal wall, which sometimes communicate with the intestine. It may also start from the vermiform appendix. There have also been cases of primary actinomycosis of the colon with metastatic deposits in the liver.

Actinomycosis of the intestines is characterized by extensive induration due to a marked development of peritoneal adhesions and to the extension of the process to the abdominal wall and neighboring organs. As before mentioned, the tendency to the formation of the fistulæ is marked. Metastatic involvement of the liver is not unusual. G. S. Towne (Albany-Med. Annals, June, 1917).

An acute or chronic inflammation of the appendix may open the door for the entrance of the actinomycotic organism. In general, actinomycosis is practically never carried by the lymphatics and but rarely by the blood stream. The method of extension is by continuity of tissue. Thus it is that general actinomycosis, unlike tuberculosis and blastomycosis, is extremely rare. Many of the abdominal organs may become involved, as extension of the process usually takes place through retroperitoneal tissues, sometimes destroying muscles and even bones.

The early diagnosis of actinomycosis is generally overlooked. A firm swelling, painless on pressure, occupying either the right or left inguinal regions, usually the right, is the sign most frequently found in intestinal actinomycosis. J. W. Keefe (N. Y. Med. Jour., Nov. 30, 1918).

There are 3 types of actinomycotic infection of the appendicocecal region, the first with a painless tumor in the right iliac fossa with ultimate formation of abscesses and fistula; the second simulating acute appendicitis, with the appendix usually found gangrenous at its base; and the third with an infected patch in the cecum, which perforates, giving rise to secondary generalized peritonitis. The writer's case was of the third type, in a woman, 32 years of age, with recurrent pain in the right iliac fossa for 2 years. Much pus was found in the pelvis and the cecum showed a thickened patch with central perforation. The normal appendix was removed, the cecal patch with its subsequent invagination was scraped, and the peritoneal cavity irrigated with saline solution by means of Carrel tubes, removed on the third day. Under **potassium iodide,** 50 grains (3.3 Gm.), 3 times a day, the wound healed, and the patient recovered. E. G. Slesinger (Lancet, June 5, 1920).

4. **Genitourinary Tract.**—The uterus may also become invaded by the disease, the first manifestation being the discharge of a turbid, fetid fluid containing the characteristic shreds and masses.

The gross macroscopic and microscopic picture resembles that of tuberculosis in many cases. Bollinger's desideratum for the diagnosis of actinomycosis, namely, that corpora flava must be present, is untenable at the present time. Repeated bacteriological examinations, and sometimes long and tedious ones, of the same specimens must be made to insure a correct interpretation of suspicious pathological material. Inoculation with pure cultures into the animal is not attended with success. Only the injection of pus with actinomycosis, or the ingestion of material upon which actinomycosis is grown, will prove successful in the production of actinomycosis in the animal. Actinomycosis does not travel by the lymphatics, and probably not by the blood route. The prognosis is favorable in circumscribed cases, which is most likely the condition in which we find the uterine appendages.

The treatment consists in radical **extirpation** and **free drainage,** the application of **tribromphenolbismuth,** or irrigation of the fistula with **copper sulphate.** The internal adminis-

tration of large doses of **potassium iodide** up to 75 grains a day, which exerts a positive healing effect. Carl Wagner (Surg., Gynec. and Obstet., Feb., 1910).

5. Respiratory Tract.—In bronchitic actinomycosis the affection is less severe in winter than in summer, which is the contrary of what is observed in ordinary bronchitis. It can be classified in three groups: (1) lesions of chronic bronchitis; (2) miliary actinomycosis, and (3) cases with bronchopneumonia and abscesses. The lower lobe is attacked more frequently than the upper; the opposite is the case in tuberculosis. Actinomycosis of the lungs is found in 20 to 30 per cent. of all cases of actinomycosis. It probably originates in the mouth, and usually takes the form of bronchitis or bronchopneumonia.

> In a personal case of actinomycosis the patient seemed to have merely pneumonia except for a tender point on one rib and this swelled a little. The surgeon was rather skeptical when called on to open this small tumor, but this revealed typical actinomycosis. Hamburger (Ugeskrift f. Laeger, Apr. 25, 1918).

6. Brain.—Here, tumor-like symptoms exist during life, with headache, paralysis of the abducens, congestion of the optic papilla, and attacks of unconsciousness. In a case reported by Ranson the autopsy indicated the probable mode of infection of the orbit and brain. A sinus was found leading from the orbit to the gum of the upper jaw; the ray fungus had probably lodged in or near a tooth, as it has so often been found to do. The fungus was probably carried into the system on an ear of corn chewed at harvesttime. Having reached the orbit, it crept along its outer wall and in the wall of the right cavernous sinus to the base of the brain, ultimately setting up meningitis and small abscesses, and burrowing through the pituitary body and sella turcica to the cavernous sinus of the left side.

> The orbit is very seldom the seat of actinomycosis. A case is reported from von Brun's clinic, and 9 cases are cited in detail from the literature. The author's case was the first to be operated upon by temporary resection of the upper part of the cheek-bone, a procedure which is considered superior to Krönlein's resection of the lateral portion of the orbit. The chief symptoms were exophthalmos and failure of vision in the affected eye. There was also lack of mobility of the eyeball. These symptoms are, however, not pathognomonic of actinomycosis, it being essential to an exact diagnosis that the ray fungus be found in the pus. As soon as a diagnosis is made, or there is a well-grounded suspicion of this disease, steps should be taken to radically remove the focus of infection. Müller (Beiträge z. klin. Chir., Bd. 68, H. 1, 1910).

DIAGNOSIS.—When the process is very rapid, actinomycosis may stimulate acute phlegmonous inflammation and osteomyelitis, or, when widespread, syphilis.

Sarcoma.—This form of neoplasm does not suppurate or break down so early.

In the jaws it is to be differentiated from dental affections: epulis.

Tuberculosis.—In this disease the lymphatic glands are infected, and the apices are usually the first involved.

In actinomycosis of the lungs the causative organism may be found in the sputum and in the discharges from fistulæ in the chest wall. In sputum the parasite is distinguished from the common leptothrix of the mouth by the fact that the filaments of the latter are larger, straighter, and thicker, do not branch, and are frequently adherent to epithelial cells.

Carcinoma.—The skin or mucous membrane involved is in close connection with the tumor; in actinomycosis the skin will be found broken on microscopical examination.

Syphilis.—A gumma will, in two or three weeks, be sensibly affected by large doses of potassium iodide, which does not act so rapidly in actinomycosis.

Lupus.—The diagnosis depends, in this condition, upon microscopical examination.

> The writer was able to differentiate actinomycosis by the seroreaction in 8 cases, the only negative reaction being in a case in which the cure had been complete for over four years. The specific reaction is both by agglutination and by fixation of complement by means of the spores of the sporotrichum. Actinomyces cultures cannot be used for the tests, but the generic reaction with sporothrix spores is constant and lively. It is specific for actinomycosis, sporotrichosis, and thrush, but these can be readily distinguished. Widal (Bull. de l'Acad. de Méd., May 10, 1910).

ETIOLOGY.—Both men and animals are probably infected from vegetables or water (Israel), from eating ears of barley, or rye, when the fungus penetrates through the wound or abrasion thus provoked, or in many cases through carious teeth. Intestinal actinomycosis is due to taking contaminated food or water, when the fungus becomes implanted upon an already diseased tissue, multiplies, and causes active proliferation of the submucous tissue. It may be transmitted by kissing, as in a case reported by Baracz. Farmers should be warned against the habit, so common among them, in chewing bits of straw, wheat, oat-chass, etc., the most prolific cause of the disease. Actinomycosis is frequently met with in shoemakers. This is due to their habit of placing their needles in their mouths (Ullmann).

The disease occurs not only in cattle, among which it gives rise to the condition known as "big jaw" or "lumpy jaw," but is met with also in hogs. In a case reported by Guinard actinomycosis of the lower jaw was acquired by a toothbrush-maker from holding washed hogs' bristles in the mouth before inserting them into the holes in the toothbrush handles.

No one has satisfactorily demonstrated the parasite out of the lesions, and nothing definite is known concerning its habitat in the outer world (Towne).

The disease occurs nearly three times as often in the male as in the female sex.

In a study of a large series of cases, Erving found the youngest case reported to have been a child 6 years old; the oldest was a man of 70. Most cases were in middle life. Thirty six per cent. of the patients had much to do with live stock or grain. In 62 per cent. of the cases the disease lasted over six months.

> The disease is a combination of abscess formation and new growth of connective tissue. In most cases the disease has the character of a subacute or chronic suppurative process, but in some cases the new growth of connective tissue may be so marked a feature of the process that it may present the character of a tumor or neoplasm. G. S. Towne (Albany Med. Annals, June, 1917).

Direct infection from the flesh or milk of affected animals, *i.e.*, from tissues or products other than the part actually diseased, does not occur, according to evidence so far obtained.

> Only 6 cases of actinomycosis of the ovary are on record, and none of these are primary. Case of the

latter kind in a patient who had lived in London for 16 years, but in 1903 and 1904 was brought into contact with hay, straw, and corn, the usual sources of actinomycosis, and it is noteworthy that the symptoms date from 1904. The streptothrix must have reached the ovary by way of the blood-stream. Taylor and Fisher (Lancet, Mar. 13, 1909).

The writer has observed a number of cases in which latent actinomycosis was roused to active proliferation by some intercurrent trauma. He has also found similar instances in the literature. There may be an interval of years between the trauma and the manifest actinomycotic process; in one case seventeen and in another ten years had elapsed, and intervals of five and ten years are by no means uncommon. Noesske (Med. Klinik, Mar. 27, 1910).

PATHOLOGY.—The actinomycoses were formerly thought to be mold fungi (hyphomycetes), but Bostroem, in 1885, proved by cultivating them that they were a variety of cladothrix, belonging to the schizomycetes.

At present the parasite is considered to belong to the streptothrix group, and the name *Streptothrix actinomyces* has been applied to it.

The actinomyces fungus can be cultivated in ordinary nutrient broth to which a few drops of fresh human blood have been added. It is advisable to sow the material in two broths, one of which is covered by a layer of oil 1 cm. deep. After incubation for a few days, the fungus appears at the foot of the tube in small white puffballs. From such a growth a vaccine can be prepared. In 2 cases in which a vaccine of the homologous organism was employed improvement resulted. Gordon (Brit. Med. Jour., Mar. 27, 1920).

The mass is made up of granulation tissue, which, except for the presence of the ray fungus, would be mistaken for a round-celled sarcoma. Epithe-lioid elements and giant cells are also seen. In the granular mass, or in the pus coming from a case of actinomycosis, the fungus itself appears under the form of small, yellow, brown, or even green masses, about a pinhead in size, which, on microscopical examination, are found to be composed of a central interwoven mass of threads, from which radiate club-shape-ended rays; in some specimens certain rays project far beyond the others. In man the clubbed bodies are frequently absent (Senn). The histological lesions are alike in the actinomycotic nodule and in the tuberculous follicle; only the foreign body differs. Water or a weak solution of sodium chloride causes the rays to swell enormously and lose their shape; ether and chloroform seem to have no action.

At a certain stage there are in every colony three elements, viz.:—

1. Club-shaped formations.

2. A centrally placed network of fungus filaments of varying shape and size.

3. Fine coccus-like bodies (spores), which originate from the fungus filaments, and grow into long rods and branching twigs.

Two types, the typical and atypical, should be recognized, according to Berestneff. Typical actinomycosis is the disease in which occur the characteristic mycelial masses, having club-shaped radiations. Atypical actinomycosis includes such diseases as Nocard's *farçin de bœuf,* and infections which clinically and anatomically resemble actinomycosis, and are caused by mycelial organisms which correspond quite closely to the cultural peculiarities of the streptothrix actinomyces, but fail to form the characteristic grains in the tissues and pus.

Case of streptothricosis, a disease of man or animal due to one of the various forms of streptothrix. The manifestations of the disease probably differ in accordance with the forms of causative organism. If organisms of thread form are present the surgeon can be reasonably sure of the diagnosis. If the threads are branched he can be certain of it. The ray fungus is seldom found in humans, and is not invariably found in bovine streptothricosis. The appearance of the disease varies with the stage in which it is seen. A description of the surface appearance of an early stage would by no means fit a well-developed or an advanced case. The appearance is greatly changed by mixed infection with pyogenic bacteria. A severe secondary pyogenic infection may obliterate all appearances suggestive of streptothricosis, and in such a case it may be impossible to demonstrate the streptothrix. Certain persistent abscesses, particularly abscesses connected with the alimentary tract, are due to streptothrix infection and secondary infection with pyogenic bacteria. J. Chalmers Da Costa (Annals of Surg., July, 1911).

Staining.—The following stains have been used:—

Wedl's orseille (Weigert).

Eosin (Marchand).

Cochineal—red (Dunker and Magnussen).

Hematoxylin alum (Moosbrugger).

Gram's method—section staining (Partsch).

Safranin in aniline oil, followed by K. I. (Babès).

Solution of orcein in acetic acid (Israel).

Picrocarmin—fungus, yellow; other parts, red (Baranski).

The actinomyces in a section are best shown by Gram's method, first with methyl violet, then with Bismarck brown (Tillmann).

Cultivation.—It is quite difficult to cultivate in coagulated blood-serum (O.

Israel), coagulated blood-serum and agar-agar (Boström), and coagulated egg-albumin and agar-agar (Wolff and J. Israel).

INOCULATION.—It has been successfully carried out by James Israel and Ponfick, from tissue and from pure cultures.

Opinions differ as to its power of producing pus, a secondary infection by the pus-germs being thought the true cause of the pus sometimes found with
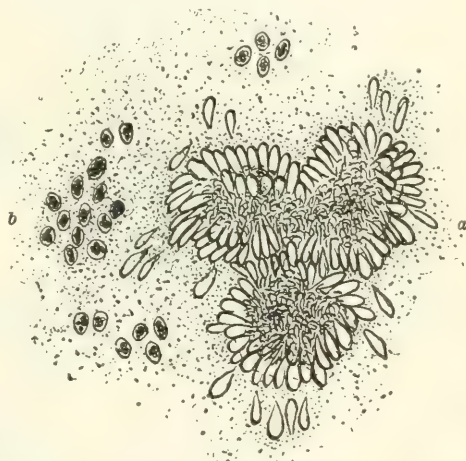
a, Ray-fungus or masses, showing central mycelium of actinomycosis. b, White blood-corpuscles, showing their relative size. (*Poncet and Bérard.*)

actinomycosis. Dissemination by the lymphatic system never occurs. Glandular enlargement indicates secondary infection.

1. Cutaneous Surface.—Around the primary lesion are small secondary lesions. Two forms are described: (a) The anthracoid, which pursues a rapid course, with fever, and sometimes septicemic in character. It is characterized by flat tumefaction, with multitudes of small openings with yellow granulations, from which thick pus exudes. (b) The ulcerofungous, which pursues a subacute course, with tendency to chronicity. In the face it tends to form

burrowing abscesses instead of recognizable tumors.

2. Bronchial Tubes and Lungs.—Some observers believe that the peribronchial lymphatic vessels and glands disseminate the fungus or its spores in the lungs; when the fungus reaches the lung-tissue proper, granulation tissue is formed, which, through secondary infection, suppurates. Amyloid degeneration of other organs may occur, or

There is widespread induration due to peritoneal adhesions, with extension of the disease to the abdominal and nearby organs, including not infrequently the liver.

Actinomycotic growths in the liver in man, according to Crookshank, have a characteristic naked-eye appearance, from their peculiar honeycombed structure. The cases between the fibrous trabeculæ are full of caseous matter, in
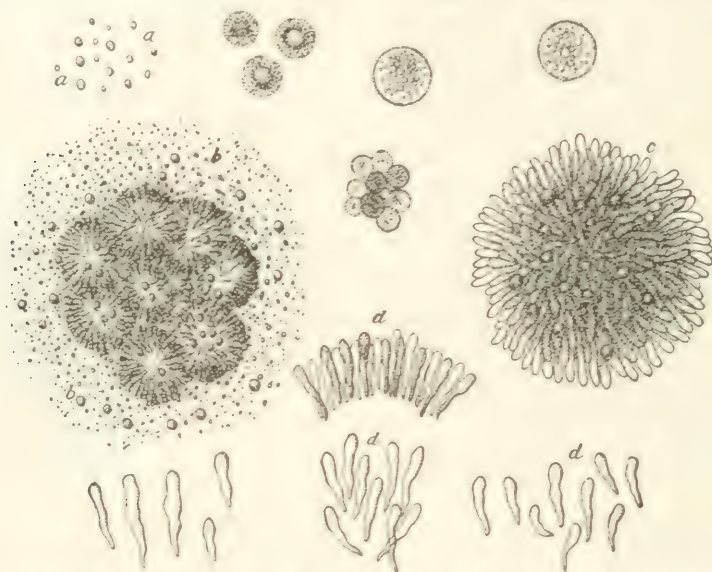
Ray fungus (*c*, *c*, *c*), club-shaped bodies (*d*, *d*, *d*), and spores (*a*, *a*, *a*) found in the pus of actinomycosis. (Perroncito and Bizzozero.)

metastasis of the disease, in case a pulmonary vein has been pierced. At times the pericardium or peritoneum becomes affected (Strümpell).

3. Alimentary Canal.—In the jaws the mass usually resembles a sarcoma, but, if incised before secondary infection and suppuration has occurred, the reddish surface will be seen to be intermingled with yellowish spots, which are collections of actinomyces.

In the intestines the fungus causes proliferation of the submucous tissue, and whitish patches. External fistulæ are commonly found.

which the more or less spheroidal masses of the fungus are imbedded. In museum specimens, which have been for some time preserved in spirit, the contents of the loculi may have fallen out, and the honeycombed appearance is then much more marked than in recent specimens.

PROGNOSIS.—The prognosis is serious in proportion to the rapidity with which suppuration occurs. Actinomycosis of the upper jaw is more serious than actinomycosis of the lower jaw, as it has a greater tendency to invade the deep structures. Internal actinomycosis

is almost always fatal, owing to its inaccessibility. External actinomycosis may cause death from pyemia, septicemia, and exhaustion. When so placed as to be easily removed and treated early the prognosis is favorable. A permanent recovery usually follows a complete removal of the primary focus, as metastasis is rare (Senn).

Actinomycosis has a pronounced tendency to spontaneous recovery except in internal organs (Schlange).

From an analysis of 60 cases the following conclusions are reached: When the disease involves the head and neck, except in a few cases when the base of the skull is invaded, the course is favorable, recovery taking place in from three to nine months. It is exceptional for the fistula to persist or to form anew after the lapse of a year. Pulmonary actinomycosis may terminate in recovery. The prognosis of actinomycosis is the more favorable, as the anterior abdominal walls are involved and the posterior escape. Death usually results from amyloid degeneration and wasting. If actinomycosis presents pyemic manifestations, a fatal termination is to be expected, as a number of vital organs are likely to be involved. Actinomycosis may pursue a chronic course, continuing thirteen years or longer, if functionally important organs be not involved, as when the process confines itself to the connective tissue about the spinal column. According to Bevan the prognosis is now much better than formerly, some cases recovering spontaneously. If surgical treatment is not possible the prognosis is grave, but not always hopeless.

TREATMENT.—1. General.—Potassium iodide was found useful in animals by Thomassen and Nocard. In man it should be thoroughly tried before surgical intervention is resorted to, especially when the disease is so extensive as to prevent complete removal by surgery. The results obtained from iodide of potassium have been remarkable in some cases and negative in others. This divergence of views, according to Pernet, depends on the variation in the virulence of the disease, in its evolution in different individuals, in the difference existing in the receptivity of the tissues, and on the influence of secondary infective processes. In recent and purely actinomycotic lesions the results may be excellent; in old-standing cases, and where the ray fungus is associated with streptococci, staphylococci, and the bacterium coli commune, the drug treatment is less successful.

According to Bérard, in two-thirds of the cases of chronic actinomycosis of the face and neck the results of iodide treatment are *nil*. In three-fourths of the recent cases recovery has been obtained by it, combined with surgical treatment, and in one-fourth by iodide treatment alone. Potassium iodide cannot be regarded as specific in actinomycosis in man. If, at the end of some weeks, improvement is slight only, operative interference should be carried out at once.

The drugs which are the most successful in pulmonary actinomycosis, in the opinion of Sabrazès and Cabannes, are **potassium iodide** and **eucalyptus**. If there is any involvement of chest wall, surgical treatment should be undertaken.

Incision alone will not cure the condition; there should also be given large doses of **potassium iodide** and a 10 per cent. solution of iodin may be injected into the region of the lesion. **Irrigation** of the **incisions** and sinuses with **diluted tincture of iodine** is also of value. Both cases

were treated in this manner and recovery was fairly prompt with little scarring. E. D. Telford (Brit. Med. Jour., Oct. 9, 1915).

The injection of a 5 per cent. solution of **permanganate of potassium** into the cysts has been of advantage.

> Six cases of actinomycosis apparently cured by injections of **sodium cacodylate.** On the first day a 10 per cent. watery solution (¼ of a Pravaz syringeful) was injected intramuscularly in the nates, increasing each day ¼ syringeful until a full syringeful is given during one week, and then decreasing the quantity to the ¼ syringeful, and then commencing over. The local measures are confined to **puncture** or little **incisions** for abscesses. More extensive operations are avoided. Foederl (Zentralbl. f. Chir., Bd. xxxv, p. 45, 1908).

> Many cases remain uncured no matter what is done. Such a severe case was treated by the writers with daily subcutaneous injections of **sodium cacodylate,** beginning with 1½ grains (0.1 Gm.), increasing to 15 grains (1 Gm.) and then again decreasing. The infiltrated mass was incised and into the surrounding 25 per cent. **iodipin** was injected twice, the second injection being given 2 weeks after the first. In a few months the wound was completely healed with hardly a scar. Bittner and Toman (Prag. med. Woch., Nu. 27, 1913).

> Case of facial actinomycosis which was cured by the administration, at weekly intervals, of 4 doses of **vaccine,** each containing 25 million fragments. Combined with this was the opening of the abscess and its curettage with dry gauze. C. W. Dean (Brit. Med. Jour., Jan. 20, 1917).

> The writers found **methylene blue** a specific for *Actinomyces* in the test tube, and used it in a clinical case, which cleared up under the treatment. Either **Roentgen ray** or **radium** is probably sufficient as a curative agent. Jensen and Schery (Jour. Amer. Med. Assoc., Nov. 27, 1920).

2. Surgical.—Local measures which do not completely remove the infected tissues do harm, as they frequently give rise to secondary infection, rapid extension, and death.

> The best treatment of actinomycosis in the writer's hands has consisted in the **removal of** the **primary focus,** and as much of the infected tissue as possible, with prolonged **free drainage.** Internally **potassium iodide** was given to the point of saturation. Of late he has given **copper sulphate** internally and uses a solution of it for the daily dressing of the wounds. Ramstad (Journal-Lancet, Dec. 15, 1916).

Cauterization with solid silver nitrate in actinomycosis of skin and soft parts in which suppuration and fistulous tracts have occurred possesses a specific action on the actinomycosis (Köttnitz).

3. Electrotechnical.—Two platinum needles, attached to the two poles of a constant-current battery, are to be inserted into the tumor. Through the two needles a current of 50 milliampères is to be passed, while every minute some drops of a 10 per cent. iodide of potassium solution are to be injected into the mass. The solution is decomposed into nascent iodine and potassium. This is repeated every eight days, each session lasting twenty minutes, under an anesthetic (Gautier).

Before suppuration all diseased tissues, glands, etc., should be removed and the parts, when possible, cauterized with the thermocautery.

After suppuration the parts should be treated as if they were tuberculous, curetting and packing with **iodoform gauze.**

> Two cases in which actinomycosis was apparently cured by irradiation. The second patient had been operated on repeatedly, undergoing about a year previously a partial resection

of the upper jaw. The infiltrate disappeared completely under **X-ray** treatment alone and the fistula closed. R. Levy (Zentralbl. f. Chir., Jan. 25, 1913).

Case of Heyerdahl's in which 4 cg. (⅔ grain) of pure **radium** were applied for 3 days to an actinomycosis beneath the right eye; there was complete cure in 2 months. H. E. Brunzel (Strahlentherap., vi, 1915).

X-ray treatment especially combined with **potassium iodide** has been employed in the treatment of actinomycosis but radium has been tried but little. The author formerly reported a case which was cured with **radium** after all other methods had failed. He has since had 5 other cases in which a prompt cure resulted. However, one case of actinomycosis of the breast died of the disease 4 months afterward. P. A. Heyerdahl (Trans. XI North. Surg. Congress, Goeteborg, July, 1916).

A few cases were treated by the writer with the **X-ray.** In 1 case a beneficial action was noted; in another case, which is still under treatment, an extensive spreading of the disease resulted so that the X-ray treatment had to be discontinued. Numerous small abscesses developed which had to be incised. Rövsing (Trans. XI North. Surg. Congress, Goeteborg, July, 1916).

ERNEST LAPLACE,
Philadelphia.

ACTOL, or silver lactate, occurs in the form of a white powder, odorless and almost tasteless, which is soluble in 15 parts of water. Its color is changed when exposed to the light. Applied to the tissues, it causes coagulation of the proteids, in common with the nitrate of silver.

THERAPEUTICS.—Actol has marked **antiseptic** and **disinfectant** properties, according to the strength of solution used. In solutions of 1 in 500 to 200 it is used as an antiseptic for wounds. For infected wounds it may be employed as a disinfectant in stronger or even saturated solutions. But little discomfort is caused when the powdered silver lactate is applied to open surfaces. It

is claimed to have a deep-seated effect by penetration to the subjacent tissues, though known to be decomposed into other compounds when in contact with the superficial cells. Actol has also been used internally as an antiseptic. It has been found effective in diminishing intestinal putrefaction, at the same time causing a tendency to constipation. Some have even employed it internally and hypodermically for a general antiseptic action throughout the organism. Sixteen grains (1 Gm.) have been injected subcutaneously without serious results. S.

ACUPUNCTURE.— This procedure is principally used for the relief of tension in edematous or congested tissues. It is especially useful in edema of the scrotum, labia, and extremities when the tissues are sufficiently distended to threaten sloughing. Acupuncture is also employed for the relief of pain in neuritis and muscular rheumatism, especially in sciatica and lumbago; the benefit afforded, when such is obtained, is due mainly to reflex contraction of the blood-vessels of the area, thus reducing the congestion of the nervi nervorum and the sensory terminals to which the pain is due. In edema, the benefit is the direct result of the abstraction of considerable blood-serum imprisoned in the tissues.

TECHNIQUE. — The instruments employed are a very small narrow-bladed bistoury and surgeons' needles. The part should be carefully sterilized by first washing it with soap and water and then bathing it with alcohol or a 1:2000 solution of mercury. The operator's hands and instruments should likewise be carefully sterilized. These precautions are very important in view of the fact that edematous tissues are readily infected. If the patient is very sensitive to pain, the part may be anesthetized with ethyl chloride.

For **edematous tissues** the small bistoury is the better instrument, one or two stabs, or, in large areas, many such, being practised, avoiding blood-vessels. A compress dipped in a warm 5 per cent. solution of boric acid is then applied to encourage escape of the serum. These must be frequently changed and the tissues kept very clean, as otherwise fetor soon appears.

For **muscular rheumatism,** especially **lumbago,** a number of round needles are thrust

into the painful area from 1 to 2 inches, according to the fat overlying the part, and left *in situ* from five to ten minutes. The pain often ceases at once. Great care should be taken, on withdrawing the needles, not to break them, lest fragments remain in the tissues. In **neuritis, sciatica,** etc., the needles, several of them are thrust into the nerve sheath at intervals (not a difficult procedure in large nerve) and left *in situ* about five minutes. A fine hypodermic needle may be used, among the ordinary needles, with advantage, in the same way, and increase the efficiency of the treatment by being used to inject a little sterile water, which acts as an analgesic, or, if the pain be very severe, morphine. This treatment is efficacious in most instances where other measures have failed.   S.

ACUTE RHINITIS, OR ACUTE CORYZA.—DEFINITION.—

An acute inflammatory condition of the nasal mucous membrane, in which repeated attacks predispose to the extension of the inflammation to the neighboring cavities, as the pharynx; the larynx; the lower air passages; and to a lesser degree, to the accessory sinuses of the nose.

A careless sneezer and the person who does not cover his mouth and nose when he coughs are breeders of acute coryza. The organisms which cause colds are so small that a million could rest on the head of a pin. When a person coughs or sneezes, a fine spray carrying with it untold numbers of these germs is spread into the surrounding atmosphere to a distance of several feet, and may be easily taken into the mouth and nose with the respired air. More direct contact, such as by kissing, the common drinking cup, the common roller towel, by pipes, toys, pencils, fingers, food and other things which have been contaminated by the mouth and nose secretions of a person having a cold also carry the disease. Rucker (Pacific Med. Jour., Oct., 1917).

Common colds of the ordinary type are infectious. It has been demonstrated experimentally that the virus of common colds occurs in the nasal secretions; and that this virus is capable of passing through Berkefeld filters which are impermeable to ordinary bacteria. By the employment of special anaërobic methods the virus of common colds has been cultivated in vitro by the writer, and has proved capable of repeated recultivation in subcultures. Experimental inoculations have demonstrated that Berkefeld N filtrates of subcultures of the virus, in the second generation at least, are infective. Another minute micro-organism has been isolated from cultures made from filtered nasal secretions in common colds. This micro-organism can be passed through Berkefeld N filters, and has been recultivated from culture-filtrates. Although conclusive proof of its nature has not been adduced, the experiments suggest that the micro-organism described bears a definite relation to the true infective agent. Analysis of the results of the writer's experiments showed that of the ten men inoculated, seven developed clear cut and definite symptoms of acute coryza; two reacted questionably, while one remaining case exhibited no symptoms. G. B. Foster (Jour. of Infect. Dis., Nov., 1917).

SYMPTOMATOLOGY.—The earliest manifestation of an acute rhinitis is a sensation of dryness or irritation in the nose, which later becomes of an itching, tickling, or stinging character. Very often the attack is ushered in by a preliminary chill or "a creepy feeling." Sneezing is an early symptom, and is soon followed by a sensation of fullness in the nose, with subsequent obstruction to nasal breathing, and a dull throbbing headache over the site of the accessory cavities. A general feeling of illness, with aching in the limbs and back, frequently prevails. The sense of smell

and taste are interfered with. Hearing is often markedly impaired, owing to the involvement of the mucous membrane at the orifice of the Eustachian tube, or the extension of the inflammation through the tube into the middle ear. The voice is also altered and assumes a nasal intonation. There is a noticeable loss of resonance which characterizes the normal voice, and the sounds of *m* and *n* cannot be readily produced. The skin is dry and at times becomes hot from the presence of fever.

Thirst and anorexia are also associated symptoms. The urine is scant and high colored. The existing constipation is usually responsible for the presence of the furred tongue. The eyelids are more or less swollen from the existing congestion, and a profuse lachrymation is not infrequently present from the extension of the inflammation through the nasolachrymal duct. The membrane of the nose is red, swollen, dry, and glazed, and is unduly sensitive. The nasal passages are practically occluded by the swelling of the membrane and the erectile tissue of the turbinates to the capacity of the fossæ, thereby greatly interfering with the normal physiological functions of the nose, as well as with that of deglutition. Owing to this existing obstruction, nursing infants at times manifest considerable difficulty in obtaining sufficient nourishment.

The nasal discharge at first is scant, or it may be entirely absent, but it soon becomes copious, is clear, and, owing to the presence of an excessive amount of salines in its composition, it becomes very irritating to the skin of the upper lip and the nasal alæ; in fact, the irritation not infrequently becomes so marked as to cause excoriation, or even cracking, of the bordering cutaneous surfaces. This condition, no doubt, is often very much aggravated by the frequent use of the handkerchief.

As the disease progresses, the discharge becomes opaque, mucopurulent in character, thick and tenacious, and of a greenish-yellow color. A microscopic examination of the discharge shows a marked increase in the corpuscular elements.

No sharp line of demarcation exists between the second and the terminal stages of this disease. In three or four days the discharge gradually becomes thicker and scantier; the swelling of the membrane subsides; the constitutional manifestations gradually lessen and finally disappear; the special senses assume their normal activity, and in the course of a week or ten days all traces of the disease disappear.

A significant feature of acute rhinitis is the possibility of the antrum of Highmore, the frontal sinus, the ethmoid or the sphenoid cells, the Eustachian tube, or the middle ear becoming the seat of disease as the result of the extension of the inflammatory process. The nasopharynx and the pharynx invariably become involved, partly through the extension of the inflammation by continuity, and partly from the interference with the normal function of the nose.

DIAGNOSIS.—The recognition of this condition, as a rule, is seldom fraught with many difficulties, and the diagnosis in most cases is usually made with considerable ease. It is important, however, to guard against the possibility of a mistake by making careful inquiry into the history of the attack, and also by making a cautious examination of the nasal cavities in order to distinguish between a simple acute catarrh and a rhinitis as the result of measles, influenza, nasal diphtheria, hereditary

yphilis, a foreign body, a tumor, and iodism. Cases of measles and influenza will invariably show a higher temperature and greater constitutional disturbances, and in the former case the appearance of the rash will eliminate all doubt of the cause of the existing nasal condition. Nasal diphtheria can be recognized by the existence of the characteristic grayish membrane in the anterior nares and in the throat, associated with the usual constitutional symptoms. In the absence of the membrane, strong evidence of the condition continues to exist in the blood-tinged discharge, but a positive diagnosis can be obtained only by culture. The "snuffles" of hereditary syphilis is usually found in very young children, with concomitant symptoms of this infection, *i.e.*, malnutrition, glandular enlargement, and in older children the characteristic Hutchinson's teeth. A foreign body or a tumor can be detected on examination, and in cases of iodism a careful history will elicit the fact that a considerable quantity of the drug has been taken.

Cases of acute rhinitis are occasionally encountered in which the causative agent is some chemical irritant. The diagnosis should not be difficult, as constitutional symptoms are rarely present; the duration of the attack is seldom, if ever, as long as the ordinary cases; and with the withdrawal of the cause the condition invariably subsides.

The patient seldom seeks treatment for acute rhinitis much before the end of the first or the beginning of the second stage of the disease, and then gives a history of exposure, quickly followed by the nasal discomfort and the rapid development of the disease. This history, in conjunction with the more or less characteristic appearance of the conditions within the nasal chambers, will usually be sufficient evidence for a positive diagnosis.

ETIOLOGY.—Predisposing Causes. —If careful observation were made in each case of acute rhinitis, it would, no doubt, frequently be seen that the attack occurs when the resisting powers of the body are below par. Under normal conditions a certain equilibrium is maintained for the production and the elimination of the waste products of the body; but, when, for some reason, the normal function of this apparatus is interfered with and there occurs a faulty elimination of the waste products or an overproduction of the same, body resistance is lowered and susceptibility to disease becomes more marked. This condition is undoubtedly often encouraged by indiscreet action of the patient in regard to diet, causing digestive disturbances, torpid liver, and constipation, in which the consumption of food is out of proportion to the combustion, thus causing an autotoxemia, in which there is sometimes a marked evidence of uric acid. It is at this time that a coryza may be considered the nasal signal of systemic poisoning, for the blood will be found tainted with the products of faulty oxidation. Strong evidence of this condition will also be found in the urine, in which uric acid or mixed urates will be present.

With such lowered resistance, one becomes easily affected by conditions such as prolonged confinement in an ill-ventilated room, extreme physical exhaustion following overwork, or a severe mental strain. A lowered nervous tone; interference with the normal activity of the sudoriferous glands, and the absence of a natural covering for the head, as in baldness, are ofttimes important predisposing factors.

It is not uncommon to find in some patients showing a disposition to frequent colds some underlying pathological condition within the nose, such as deviation of the septum, a stenosis, or a hypertrophic rhinitis, thus causing the current of air to be misdirected in such a way as to act as an irritant upon a more or less sensitive membrane, which is usually below par as the result of recurrent attacks.

When frequent and persistent attacks occur in childhood, a careful examination of the nasopharynx will sometimes show the causal agent to be the existence of adenoids. Acute rhinitis is not infrequently found in infants under three months and those who are suffering from malnutrition, as in rachitis. It is also thought by a noted pediatrist to be a complication of dentition. In susceptible children, the cause is often very trivial. A curious fact exists in that this affection is seldom found in old people.

An hereditary tendency seems quite apparent in some cases, notably in children. In the majority of cases, however, the direct cause can be traced to an improper mode of living. The child gets very little fresh air; is confined in a room which is improperly ventilated, usually overheated; the windows of the bedroom are kept carefully closed at night for fear the child may catch cold; the clothing is very often in excess of what is really needed, thus making it impossible for the individual to indulge in any active play without producing a profuse perspiration. Under these conditions the mucous membrane, especially of the nose and throat, soon becomes very sensitive and the child is a frequent sufferer of colds

Evidence sometimes points to such chronic conditions as asthma, hay fever, rheumatism, tuberculosis, and syphilis as being factors in the production of acute rhinitis. Attacks in some persons can be attributed only to their idiosyncrasy. Excessive sexual indulgence often shows a predisposition to provoke an attack, as do gastric and intestinal diseases, and a neurotic tendency. Thermic and climatic conditions are sometimes to be considered.

The writer inclines to the theory of the nasal mucosæ in coryza as eliminators of substances resulting from faulty metabolism. Hagemann (Med. Rec., Feb., 14, 1914).

The most potent general cause of colds in intestinal poisoning of a chronic nature, which leads to an alteration of the vasomotor control, with the possible addition of a local cause to keep this active. Local causes may be divided into two classes, malformations of the nose, and chronic disease of the frontal sinuses; then there is the cold which is simply the manifestation of a general condition, such as grippe. The ordinary cold in the head is most often due to bacterial infection. J. G. Dwyer (N. Y. Med. Jour., May 11, 1918).

Exciting Causes.—Although certain depraved conditions of the body may be said to predispose to attacks of acute rhinitis, usually there are certain causes to which the attack may be definitely attributed. Exposure to cold and wet when the body is overheated; exposure to sudden or extreme changes in the atmosphere; the wetting of the feet when the system is debilitated from other diseases; or the chilling of the body from any cause, especially as the result of sitting in such a position as to allow a draft of air to strike the back of the neck or head. This seems to support the theory advanced by some that the impression of cold on certain parts of the body produces an inhibi-

tory effect upon the vasomotor nerves controlling the blood supply of the nasal mucous membrane.

The inhalation of certain irritating chemical fumes, such as those of iodine, chlorine, bromine and hydrochloric acid may result in a coryza. Sometimes the mere inhalation of irritating dust may produce an attack. Foreign bodies in the nose; or certain drugs, as ipecac and the iodides, may produce the same effect. Wagner is of the opinion that the inflammation is not infrequently the result of migration of bacteria from diseased tonsils. The examination of the nasal secretion often shows the presence of a variety of micro-organisms, chief among which are the *Micrococcus catarrhalis,* the *Bacillus septus,* the *Bacillus Friedländer,* and the *Bacillus segmentosus* of Cautley.

> The evidence seems indicative that the diphtheroids, particularly *Bacillus segmentosus* of Cautley, are concerned in the production of common colds. The *Micrococcus catarrhalis* is much more general in its manifestation, and is, probably, also epidemic and productive of a rather more severe inflammation. It seems likely the symbiosis of these 2 organisms increases the virulence. The pneumobacillus of Friedländer is much more concerned in chronic conditions and is probably identical with the ozena bacillus. The pneumococcus of Fränkel flourishes in any part of the upper respiratory tract and, when virulent, has been found in pure culture. Clinically, the segmentosus infection is most likely to be in the nose, seldom in the trachea, but may cause otitis media; *Micrococcus catarrhalis* is most apt of all to invade the larynx and trachea. W. Walter (Jour. Amer. Med. Assoc., Sept. 24, 1910).
>
> The writer reports having discovered in acute and chronic rhinitis a Gram-negative anaërobic organism (*Bacillus rhinitis*), which he regards as the exciting cause in at least some

cases of coryza. Tunnicliffe (Jour. Amer. Med. Assoc., June 28, 1913).

> Experiments by the writer strongly suggested that the causative virus is ultramicroscopic and filterable, the clear filtrate obtained from passage of diluted coryzal secretions through a Berkefeld N filter, and even subcultures from this filtrate, causing rhinitis when dropped into the nostrils of healthy subjects. G. B. Foster, Jr. (Jour. Amer. Med. Assoc., Apr. 15, 1916).
>
> The literature shows no convincing evidence that any known organism is the primary cause of the common cold. Cultural studies fail to show in uncomplicated cases any variation in the flora which would enable one to select any organisms as the cause of colds. On the other hand, where clinical complications occurred, pathogenic organisms were definitely associated with them. The writer feels, therefore, that the primary cause of colds is probably an organism as yet unknown and certainly not one of the usual pathogens such as a streptococcus, pneumococcus, *B. influenzæ* or staphylococcus. But the primary cold, whatever its final cause, alters the mucous membranes in such a way as to allow secondary bacterial invasion and consequent frequent development of local complications. The cultures clearly indicate that such complications are due to a variety of bacteria, such as pneumococcus, streptococcus, and staphylococcus. Bloomfield (Johns Hopkins Hosp. Bull., Apr., 1921).

Whenever the disease is at all prevalent, suspicion arises as to the possibility of it being contagious or produced by some infectious material in the air. It not infrequently ushers in an attack of bronchitis, laryngitis, or one of the acute infections, such as influenza, measles, typhoid fever, small-pox, or whooping-cough.

PATHOLOGY.—An acute rhinitis is characterized by the same pathological changes which take place in in-

flammation of the mucous membrane elsewhere in the body, and may be considered in three stages.

Stage of Engorgement.—During this stage the mucous membrane is swollen and rather dark in color. The normal secretion at first is decreased, or even entirely arrested, and there occurs a proliferation of the epithelium. If the microscope could be used at this time, the blood-vessels would be seen to be markedly dilated and there would be more or less stasis of the blood-stream, permitting the adhesions of leucocytes to the blood-vessel walls. Their final penetration into the surrounding tissue is the beginning of the next stage.

Stage of Exudation.—With the migration of the leucocytes into the interstitial tissue, there is also a transudation of altered blood-serum and a forcing out of erythrocytes. The discharge that follows is usually profuse; at first it is a mixture of mucous and serum, but this soon becomes of a mucopurulent type and finally purulent.

Stage of Resolution.—This is characterized by the restoration of the normal function of the mucous glands, the secretion from which causes the discharge to become thicker and more opaque. The exudate within the mucosa is gradually absorbed, the lost epithelium in time is replaced by new cells, and the membrane is slowly reduced to its normal size.

PROGNOSIS.—This depends upon the severity of the attack and the extent to which the tissues are involved. The simple cases usually recover in the course of a few days to a week without any detrimental results. In some few cases, however, certain changes may take place in the tissues and increase their tendency to recurrent attacks. The prognosis becomes less favorable for an early recovery if the inflammation should extend into any one of the accessory cavities of the nose and cause a suppurative process, or if there should occur an involvement of the middle ear by extension through the Eustachian tube.

TREATMENT.—The treatment of acute rhinitis may be prophylactic, abortive, or curative, depending upon the cause of the attack. Persons who show a predisposition to recurrent attacks of coryza should guard the body against such conditions as favor their onset. The protective agencies of the body should be strengthened by regular and systematic exercise, especially in the open air, and should be of the nature of horseback riding, golf, tennis, or something as vigorous. Grayson recommends, instead of medicine, good **vigorous exercise** several times a day, claiming that "the quickened capillary circulation and vigorous action of the sweat glands that accompany hard exercise are incomparably more beneficial than the merely passive leakage that follows the use of diaphoretic drugs. If in addition to this an **abundance of water** is drunk and the supply of **food** is greatly **reduced**—almost stopped in fact—we may look for an amelioration of all the coryza symptoms in a much shorter time than if our main reliance is vested in quinine, belladonna, and opium combinations, that have had too long a vogue."

Proper **discretion in diet** should be practised, particularly by those who are victims of uric acid diathesis. **Cold bathing,** gradual at first, is an efficient stimulant to the relaxed vascular system. Proper selection of underwear and clothing, especially for outdoor service, should be made.

If the patient is seen in the early

stages, in the first few hours, the attack may be abbreviated, or the duration, at least lessened, if the proper treatment is immediately instituted. The patient should be given a **mustard foot-bath,** 4 grains of **quinine,** 10 grains of **Dover's powder,** a hot lemonade, and then put to bed with a liberal covering of bedclothes to encourage free perspiration. This should be followed by active **catharsis.** The above treatment will usually necessitate the keeping of the patient in the house at least the following day. **Aspirin** is considerably used, often with benefit.

Recent investigations lead to the belief that the isolation of the predominating organism from the nasal secretion and the injection into the patient of a **vaccine** product from the same will frequently abort an attack, and even establish a certain degree of immunity for a short period of time. The earlier the injection, the more decided will be the result. A **mixed bacterial vaccine** is recommended by A. P. Hitchens. (See BACTERIAL VACCINES, this volume.)

> By means of **vaccine** therapy, not only are we able to cut short an acute cold, but also to confer considerable immunity against future attacks. By this method we can, further, often successfully treat colds which have become chronic, *e.g.,* chronic rhinitis, laryngitis, bronchitis, etc.
>
> In but few cases of common cold can a stock vaccine be employed with much hope of success; except in the case of the *Bacillus septus* we are not likely to do good by any vaccine other than that prepared from the patient's own person. Having secured the specimen it is forwarded to an expert, and the vaccine can be prepared ready for use within forty-eight hours of its receipt. The best time for the injection is the evening, and the best spot the flank slightly above and internal to the an-

terior superior spine. If the reaction is pronounced it may be necessary to keep the patient in bed for twenty-four hours. Campbell (Practitioner, Oct., 1909).

The immunity obtained lasts, on the average, from 4 to 6 months. In those subject to recurrent colds in winter an **autogenous vaccine** should be made from the first cold, to which may be added other stock "cold germs": staphylococcus, 400 to 800 million as the full dose; pneumococcus, M. catarrhalis, and M. tetragenus, of each 125 million; B, influenza, B. septus, and B. Friedländer, of each 100 million; and streptococcus, 50 million. Eight minims (0.5 c.c.) of the vaccine should contain the required number of sterile germs. The vaccine is given in increasing dosage at weekly intervals until 4 to 6 doses have been administered. J. W. Fisher (Boston Med. and Surg. Jour., June 5, 1913).

The writer recommends the taking of an X-ray plate of the sinuses in the headaches and neuralgia incident to coryza, especially recurrent cases, and the use of **autogenous vaccines** in treatment. His rule in vaccine treatment is to begin with 3 minims of vaccine followed by 5 minims at the end of 48 hours if there is no reaction, and then gradually to increase up to 10 minims, avoiding a reaction if possible. H. I. Fifield (Med. Rec., Mar. 10, 1917).

Early convalescence and the return of the normal vigor will be augmented by the administration of **tonics,** strychnine and quinine being two of the favorite remedies. After two or three days this treatment is not sufficiently efficacious and curative measures will have to be resorted to.

The usual run of cases can be cured without confining the patient to the house, unless the weather is severe. In children, however, an attack which may be considered mild in an adult may be severe enough to confine the young

patient to bed. On the first visit of a case of acute rhinitis, especially if early in the disease, the nasal discharge will be found thin and acid, and the mucous membrane markedly swollen. Reduction in the size of the turbinal bodies can be obtained by the application of a 1 per cent. solution of **cocaine** and a 1 : 10,000 solution of the **suprarenal extract**.

A solution of 2 per cent. **cocaine** and 2½ per cent. **antipyrin** often acts to greater advantage in these cases, as the latter remedy prevents a violent reaction and frequently prolongs the contraction.

In patients who are sufferers from gout, the **cocaine** will invariably fail to produce the desired reduction of the mucous membrane, but relief may be obtained by the free administration of **colchicum**.

Cocaine should be used with the greatest care in infants, as they are particularly susceptible to its detrimental effects. Weak solutions are permissible, however, when the symptoms are severe and the infant is prevented from nursing. Powders containing **cocaine** are often prescribed for adults; but it has caused cocainomania in so many cases that it should only be applied by the physician himself with an insufflator to cause contraction of the mucosa and the effect kept by means of a powder containing no cocaine which can be used as snuff.

For use by the physician the following is efficient:—

R Cocaine hydrochloride,
Camphor ....āā gr. j (0.065 Gm.).
Pulverized sugar.... ʒij (8 Gm.).
Morphine hydro-
    chloride .... gr. j (0.065 Gm.).
Pulverized acacia,
Bismuth subnitrate.āā ʒj (4 Gm.).
Pulverized mallow... ʒiss (6 Gm.).

Enough to cover a dime to be insufflated in each nostril.

Ointments may also be used conveniently by the physician, by means of a flat probe. Lemoine recommends the following formula:—

R Cocaine hydrochloride,
Salol ....āā gr. ⅓ (0.021 Gm.).
Menthol .... gr. ss (0.032 Gm.).
Boric acid .... ʒss (2 Gm.).
Petrolatum .... ʒj (30 Gm.).

A piece the size of a large pea is applied with the probe to the swollen mucosa in each nostril.

Insufflations may be made with:—

R Calomel,
Morphine hydro-
    chloride ....āā gr. ⅙ (0.01 Gm.).
Bismuth subnitrate .. ʒiiss (10 Gm.).

To sustain the effect Rudaux, Grosse and le Lorier recommend the instillation into each nostril, night and morning, of several drops of the following solution:—

R Eucalyptol .... gr. ⅘ (0.05 Gm.).
Sterilized liquid
    vaselin .... ʒj (30 c.c.).

On the other hand, Weitlauer, of Innsbruck, commends the internal use of sodium salicylate, combined with Dover's powder, which, it is said, will afford relief one hour after beginning treatment:—

R Sodium salicylate..... ʒj (30 Gm.).
Dover's powder ...... gr. xlv (3 Gm.).
Spirit of peppermint... ♏j (0.06 c.c.).

To be divided into 20 powders, 1 of which is to be taken in a little water every three or four hours.

Where obstinate coryza results from chemical irritation of the mucous membranes, the writer recommends the following solution:—

R Sodii sulphidi... gr. lxxx (5.3 Gm.).
Glycerini .... ʒiiss (75 Gm.).
Aquæ destillatæ.. ʒvj (25 Gm.).
M.

The solution is used as nasal douche twice a day, one teaspoonful of it being placed in a quart (liter) of normal saline solution. G. Laurens (Jour. de méd. de Paris, May 3, 1916).

When the profuse watery discharge is very troublesome a powder consisting of 2 drams (8 Gm.) of **bismuth subnitrate**, 1 dram (4 Gm.) of starch, ½ dram (2 Gm.) of gum arabic, with 2 drams (8 Gm.) of **menthol**, or 10 grains (0.6 Gm.) of **antipyrin** may be snuffed up, and usually gives considerable relief. The writer has not been successful in the use of vaccines. If there is much headache or face pain an **adrenalin spray** of 1 to 10,000 may be employed, but this is not usually necessary. Ordinarily after the alkaline spray the following spray is used:

R *Acidi carbolici*. ℥x (0.6 c.c.).
  Iodine,
  Kalii iodidi
    pip ....āā gr. vj (0.4 Gm.).
  Aquæ menth.
    āā .... ℥ss (15.0 c.c.).
  Glycerini aquæ
    q. s. ad .... ℥iij (90.0 c.c.).

This is sprayed until it reaches the throat. After this an oil spray of the following composition is employed for about 10 minutes:

R *Ol. cloves* .... ℥x (0.6 c.c.).
  Camphomen-
    thol .... gr. xxiv (1.5 Gm.).
  Ol. pini syl-
    vestris ...... ℥xx (1.2 c.c.).
  Liq. petrolati
    q. s. ad .... ℥iij (90.0 c.c.).

These measures are not expected to destroy all of the germs, but to lessen their virulence and to provide drainage. When the infection has reached the bronchi, expectorants alleviate symptoms and hasten recovery. If the nose is treated in addition in the way outlined the patient recovers in a little over half the time required when only internal medication is employed, and is able to attend to his business during the attack. T. F. Reilly (Amer. Jour. Med. Sci., May, 1917).

Aromatic spirit of ammonia and **sweet spirit of niter** are recommended as excellent agents to "abort" a cold by Beverley Robinson. A couple of doses of **acetylsalicylic acid** are also helpful.

One or two doses of 1 Gm. (15 grains) each of **acetylsalicylic acid**, taken at the first indication of an oncoming cold in the head, will arrest it. The drug is especially effectual when the first tickling in the throat is felt toward evening, and the drug is taken then and again in the morning. This permits him to go about his surgical tasks after breakfast without any further symptoms of coryza. If acute rhinitis has developed or the coryza relapses, two or three further doses always cured it completely. The drug probably does not act on the bacteria, but it seems to enhance the resisting powers of the tissues. Sick (Münch. med. Woch., July 16, 1912).

The writer emphasizes the remarkable power of **bicarbonate of soda** in arresting a "common cold." About ½ teaspoonful in ⅓ of a tumbler of water, is repeated each half hour until 4 doses are taken. If the cold returns the same treatment causes it to cease permanently. L. Duncan Bulkley (Med. Record, Oct. 19, 1918).

The administration of **dionin**, in ½ grain (0.03 Gm.) doses, once or twice daily, has been recommended.

At home the patient should be instructed to use one of the well-known cleansing sprays, such as **Dobell's solution, glycothymoline,** or a solution made from **Seiler's tablets.**

A very useful and economical solution is prepared by dissolving a teaspoonful of salt in a pint of water—practically a **normal salt solution**—and using it freely in the nose.

In using any cleansing solution, great care should be exercised in blowing the nose directly afterward, for when it is done too harshly some of the solution mixed with the nasal secretion may be

blown into the middle ear through the Eustachian tube and set up an inflammation with the formation of an abscess.

Following the cleansing, the inflamed mucous membrane may be protected by an oily solution composed of :—

R Menthol,
    Camphor ....āā gr. v (0.3 Gm.).
    Liq. albolene.......... f℥ij (60 c.c.).

This is to be sprayed in the nose, or several drops may be placed in each nostril, and snuffed up, several times a day. If it is found impossible to drop the solution in the nose of a child, the application may have to be made by a brush.

Another useful combination is :—

R Menthol .... gr. viiss (0.5 Gm.).
    Phenylsalicylate .... ʒss (2.0 Gm).
    Boric acid .... ℥ij (8.0 Gm.).
M. fiat pulvis.

Since the swelling of the mucous membranes renders the snuffing up of the powder difficult, the patient will find it advantageous to use a piece of rubber tubing about 20 cm. long; the powder is placed in it at one end, and air blown through from the other end by the mouth.

An excellent agent to keep the swelling of the mucosa down is the **adrenalin ointment** 1 : 1000, a piece as large as a pea being applied in each nostril.

During the early stage of the disease, when the nasal discharge is watery, one of the coryza tablets on the market can be used to good advantage to dry up the excessive secretion. This is particularly advantageous to those who are compelled to appear in public. A very satisfactory combination is the one devised and recommended by Dr. S. MacCuen Smith, which is made up as follows :—

R Atropine sulphate .... gr. 1/600 (0.0001 Gm.).
    Strychnine sulphate,
    Arsenous acid . āā gr. 1/240 (0.00027 Gm.).
    Morphine sulphate .... gr. 1/100 (0.0006 Gm.).
    Quinine sulphate. gr. 1/10 (0.006 Gm.).
    Powd. camphor. gr. 1/4 (0.016 Gm.).

By the time six of these are taken, at half-hour intervals, a dryness in the throat will be noticed. Only half of one should be given to a child of five years. Notwithstanding their known value among the laity, the indiscriminate use of these tablets should not be encouraged, for their administration at a time when the nasal discharge has become inspissated renders the patient much more uncomfortable and the discharge more difficult of expulsion.

In the third stage, when the membrane is relaxed and the epithelium is being shed more rapidly than it should, a spray composed of 20 to 60 minims of the distilled **extract of hamamelis** to the ounce of water may be used to good advantage.

It seems almost needless to state that the **diet** in all cases of acute rhinitis should be restricted at the beginning of the attack, but as convalescence takes place it can gradually be increased and finally restored to its normal status.

In those cases, and especially is this true in children, where there is a tendency to excoriation of the upper lip and the nostril, these exposed cutaneous surfaces should be protected from the irritating effect of the discharge by the application of **vaselin** or some simple ointment.

Sodium salicylate causes a cold to abort if taken within twenty-four to thirty-six hours. Single dose of 7½ grams (0.5 dram) often suffices. Taken later, it relieves symptoms and shortens attack. It is also valuable in the chronic coryza of gouty sub-

ice. Served in these after solu-
... proximity or small doses, dis-
... that 2 grammes of water
... dissolved in twenty-four ...

The following spray recommended ...

... M.

... Mai 2, 1977)

... E. Spalteholz,
Philadelphia.

ADDISON'S DISEASE.—In 1855,
Addison printed out in a famous mono-
graph ("On the Constitutional and
Local Effects of Disease of the Supra-
renal Capsules") the relation between
a disease known as "bronzed skin" or
"bronzed cachexia," and lesions of the
adrenal bodies. The interest excited
by this work at once called forth nu-
merous observations on the subject,
and, while a certain number of the
reports bore support to the idea of close
relationship between the lesion of the
adrenals and the syndrome which Addi-
son described, in others a contrary
opinion was expressed. In the year
succeeding the publication of his first
monograph, Addison brought out a
paper in which he described a lesion of
the semilunar ganglia unaccompanied
by changes in the adrenals.

We can thus state that it was Addi-
son himself who originated the two
theories which are still brought into
requisition to explain the manifesta-
tions of the bronzed disease: the
theory of adrenal insufficiency and the
nervous theory. Before discussing
these theories a study of the dis-
ease itself from the clinical aspect
must first be made.

SYMPTOMS. — When Trousseau
proposed that the term "Addison's dis-
ease" be applied to the affection de-
scribed by the Scotch physician under
the name "bronzed skin," he specifically
designated "a singular cachexia espe-
cially characterized by the bronzed
hue assumed by the integument." We
therefore feel justified in including
under the term Addison's disease only
those affections which are of the
"bronzed disease" type, and not the
aggregate of all the conditions resulting
from functional disturbances of the ad-
renals, i.e., "without melanoderma, no
Addison's disease." The disease, even
thus limited, still presents a number of
clinical forms showing rather well-
marked special characteristics.

The writer has encountered a num-
ber of cases in soldiers which would
have been classed with the traumatic
neuroses if it were not for the fact
that the men presented certain symp-
toms which we are accustomed to
encounter with Addison's disease,
especially the pronounced browning.
Analysis of the cases shows further
a deficiency in the functioning of
both parts of the suprarenals, but
there are no manifestations of tuber-
culosis, no acute lymphatism, etc.
The course of the affection also is
comparatively light and several of
the men have materially improved,
while the result is all a upward.
Vaincheim (Deuds Nrach. ...
No. 3, 1917).

Anatomy.—The patient is generally
unable to state the exact period of on-
set of the affection. In typical cases
the pathological seat is almost always
one of adrenal tuberculosis, which has
invaded these organs secondarily, the
patient is already in the second stage
of tuberculosis, and it is difficult to
recognize the new symptoms. Where
there is primary adrenal tuberculosis,
however, the symptomatology is more

characteristic. Asthenia dominates the whole picture. The least physical effort is followed by extreme lassitude. At first the patient is still capable of energetic and rapid muscular activity, but he is not equal to sustained work; fatigue at once appears; later, as the process advances, lassitude becomes constant and the patient thinks of but one thing—avoiding the slightest exertion and remaining in bed in the dorsal decubitus. The mere ingestion of food requires an effort beyond the patient's strength, and the administration of solid food becomes difficult.

The earliest writers had been struck by the asthenia of Addison's disease, and Jaccoud gave an excellent description of it. But the exact conditions under which this fatigue occurs were learned through the labors of Langlois, Charrin, and Abelous, who explained it on the basis of a new conception of its pathogenesis. The study of muscular fatigue with the ergograph of Mosso permits of differentiating the resistance in an ordinary case of tuberculosis from that in one of Addisonian phthisis. The simple tuberculous subject will continue lifting the weight of the ergograph for two minutes, performing total work equal to 1150 grammeters; the Addisonian subject, after having lifted the weight just as energetically during the earlier contractions, becomes fatigued very soon and stops exhausted before the second minute, having performed work equal to only 750 grammeters. If the weight to be lifted is placed at 2 kg., fatigue already appears at the fifth contraction and the sum of work done is practically *nil*.

Melanodermia, or *bronzing*, from which symptom the disease received its earliest appellation, often does not develop until after the asthenia. It ap-

pears most frequently in the form of small, brownish macules scattered over the entire skin-surface, though most marked at certain points of election. The scrotum and labia majora, which are normally pigmented, very frequently present a characteristic color. The mucous membranes are very often affected before the skin. The internal surfaces of the cheeks, the labial commissures, as well as the genital mucous membranes, should always be examined in asthenic subjects.

The melanodermia may remain localized, and this is, indeed, more usually the case, but it may also become generalized through confluence of the primary patches and involve the whole of the integument, making the patient's skin appear truly like that of a mulatto, though never like that of a full-blooded negro. Brault points out that the palms and soles are not involved, but these areas are imperfectly or not at all pigmented in negroes, and even in the anthropoid apes the soles of the feet remain of a pink color.

Case of Addison's disease in a male, aged 31, in whom exposure to the sun darkened the pigmentation, which involved the axillæ, elbows, nipples, breast, the pubis, gums, lips, tongue. Of late the nails have become a dark brown. A. B. Chace (Post-Graduate, Feb., 1911).

The writers observed a case of Addison's disease in a boy, aged 12 years. A general bronzing of the skin developed radially. It was especially marked around the nipples, the umbilicus, and pudenda. There were a number of pigmented scars on the body but no buccal pigmentation. The boy developed synchronously loss of energy, drowsiness, a cough at night and nocturnal enuresis. The heart was small. An uncle and a brother are said to have had tuber-

culosis. There were no signs of pulmonary or spinal tuberculosis and von Pirquet's reaction was negative on two occasions. The skiagraph showed calcification in the adrenal glands and discrete and dense opacities at the hila of the lungs suggesting calcified nodules. The red-cell count was high, 6,492,000, and there was a high lymphocyte count supposed to be indicative of lymphatism and a bad prognosis. The eosinophiles were high, from 5 to 7 per cent. The heart was also small in this case. Rolleston and Boyd (Brit. Jour. Child. Dis., xi, 105, 1914).

Traumatism of the skin is a predisposing cause to pigmentation. The earliest melanodermic patches are often noted to appear over old cicatrices, especially over the healed areas of former blisters, and even the application of a blister or merely of a poultice on an asthenic subject is often sufficient to cause a sudden outburst of pigmentation and permit a diagnosis of Addison's disease.

Gastrointestinal disturbances are frequent, but very variable in nature. At the outset, constipation is the rule, and is accompanied by anorexia, which may be accounted for both by the intestinal paresis and by the general lassitude to which we have already alluded. The constipation may be succeeded, particularly in the acute forms, by atonic diarrhea. But the most characteristic symptom is, without doubt, vomiting. Preliminary nausea is very seldom present; the vomiting comes on suddenly, and generally in the morning upon awaking. At first the patient's stomach is evacuated but once a day; then, as the disease progresses, the vomiting becomes more frequent and occurs at intervals during the day. The act takes place with but little muscular effort, of which the subject

is, indeed, incapable. The vomitus is colorless, thin, and consists of mucous.

Circulatory disturbances are of great importance. The earlier observers had already pointed out a special weakness of the pulse, together with all the symptoms of cerebral anemia. The researches of Schäfer and Oliver and of Langlois and the later investigations of the action of adrenalin served to direct the attention of clinicians to these disorders, at the same time disclosing their pathogenesis.

The Addisonian subject is in a state of hypotonicity. By reason of the absence or insufficiency of the adrenal secretion, the normal tonus of the vessels is no longer maintained. Even at the outset of the affection, along with the first signs of asthenia, lowered arterial tension is to be found. The sphygmomanometer shows 100 to 120 mm. of mercury. The fall in pressure is accentuated as the disease advances; in the last stages, a tension as low as 50 mm. may be noted.

Bernard and Sergent have brought out a clinical phenomenon which they claim to be useful in diagnosis without the aid of instruments of precision, viz., the "adrenal white line"—as opposed to the red line of meningitis. To cause it to appear, the skin of the abdomen is lightly rubbed with the pulp of a finger, without scratching; after a few moments a rather broad white streak appears, which becomes more and more marked, remains stationary for three to four minutes, then gradually fades off.

> In cases showing rapid development there was an increase of urea— 2 grams or thereabouts—although the kidneys showed no lesions, macroscopical or histological, at the autopsy. Sicard and Haguenau (Paris Méd., May 23, 1914).

Pain and Nervous Disturbances.—Lumbar and abdominal pains of great severity may be present at the outset of the disease. They frequently become localized in the epigastric and hypochondriac regions, and Martineau has described a pathognomonic seat of pain at the anterior extremity of the eleventh rib. These pains, however, almost characteristic when they are sudden in onset, are sometimes entirely wanting throughout the course of the disease. When considering the pathogenesis of the affection, we shall find it easy to understand how the variations observed in the painful phenomena may be explained according to the extent and the seat of lesions surrounding the adrenals.

We have already mentioned the asthenic manifestations, which, according to us, are referable rather to the muscular system than to the nervous system proper, or at least to the structure which unites the nerve with the muscle—the terminal plate (as formerly designated) or the receptive substance of Langley. True paralyses are rare and in no sense characteristic. Cerebral disturbances, such as the prostration, the tinnitus aurium, the hallucinations, and especially the encephalopathy of Addison's disease, may be due to two causes: cerebral anemia resulting from vascular hypotonicity, and intoxication either through suppression of the antitoxic activity of the adrenals or through the formation of toxic products owing to functional deficiencies—asthenia, hypotonicity, etc.

General Disturbances.—The muscular and vascular weakness are necessarily followed by disorders of a general nature. The chemical interchanges are reduced, the phenomena of assimilation greatly retarded, whence result marked wasting of the tissues and a strongly manifested sensation of cold generally accompanied by hypothermia. According to the view of Sajous, who considers Addison's disease as characterized by deficient oxidation and lowered metabolism, a study of the temperature should enable us to judge of the degree of adrenal insufficiency.

The blood in cases of Addison's disease presents nothing peculiar. The search for pigment in the blood-plasma has always proved negative. Generally the blood-cells show diminution, but observations on this subject have been contradictory. While Laignel-Lavastine described diminutions of the corpuscles to three millions, Loeper and Crouzon found a polycythemia. Langlois, in a comparative study of two tuberculous cases presenting similar pulmonary lesions, but one of whom showed distinct Addison's disease, observed no difference either in the hemoglobin percentage, the number of cells or the proportion of leucocytes. The two patients gave identical results.

The secretion of urine is diminished because of the lowered tonicity. Colasanti and Bellati, who made a study of the urine of an Addisonian patient for eighteen days, found its toxicity above that of normal urine. Langlois did not find this abnormal toxicity in the two subjects of which he made a comparative study.

Course and Termination.—Addison's disease always terminates fatally, but its course may be more or less rapid. Sometimes the destruction of the adrenals is so quickly produced that the morbid phenomena show very rapid progression. Asthenia is present almost from the outset, the circulatory

disturbances at once become very marked, and, lastly, the gastrointestinal disorders, which do not appear to be closely related to the adrenal insufficiency, may become of such severity, with intractable vomiting and diarrhea, that cachexia and death supervene before the melanodermia has had time to declare itself.

In the cases having a slow course, the disease may remain stationary for a long time, and it is in such cases that are sometimes observed temporary periods of improvement not only with regard to the digestive tract, but also in the symptoms of melanodermia: asthenia and arterial tension. The cause of such periods of improvement it is difficult to state.

Combined Addison's disease and exophthalmic goiter was observed by the writers. When the suprarenal glands are insufficient, the thyroid may come to their aid, by increasing its own functioning. In 26 cases of Addison's disease they obtained a thyroid reaction in 4. In 1 of these in this group, the thyroid enlarged about 6 months after the visible onset of Addison's disease. Tachycardia, tremor and other symptoms of exophthalmic goiter became superposed; as they developed, the symptoms of Addison's disease became attenuated. This sequence of clinical phenomena was so striking, they accepted it as a suggestion for organotherapy, and since then have been giving patients with Addison's disease 0.5 Gm. (7½ grains) of pulverized suprarenal tissue and 0.01 Gm. (⅙ grain) of thyroid powder in the morning, fasting for 6 days. Then they drop the thyroid, keeping on with the suprarenal treatment for 10 days and then continuing with 10 days of the 2 combined, and so on. The outcome was not very clear in some of the cases, but in 3 the improvement was marked. Ramond and François (Jour. Amer. Med. Assoc., from Bull de la Soc. Méd. des Hôp., Nov. 16, 1917).

We shall lay no stress on the mode of death by progressive cachexia, which presents nothing peculiar, but must dwell with some emphasis upon the form of death which takes place rapidly or even suddenly.

The rapid fatal termination in Addison's disease takes on the features of an acute intoxication. The abdominal pains show marked exacerbation; diarrhea becomes profuse and vomiting continuous, the blood-pressure at the same time showing progressive reduction.

In some cases hypothermia is observed, with a tendency to collapse; in others, on the contrary, there occurs hyperthermia accompanied by delirium and convulsions.

To explain this sudden aggravation in the course of the affection, several hypotheses have been put forth. That one which appears to us the most admissible among them is based on a sudden diminution, sometimes even on almost complete suppression, of the function or rather the functions of the adrenals. Almost always, indeed, such an unfavorable turn in the disease succeeds upon an intercurrent infection. Now, since the researches of Charrin and Langlois, followed by those of Loeper and others, it has been known that certain infections, such as diphtheria and scarlatina, exert a selective action on the adrenal glands, causing in them a more or less marked functional deficiency. It is thus plain that if in a gland already the seat of tuberculosis, but which, nevertheless, suffices to insure the adrenal function, a fresh lesion appears to destroy the surviving cellular elements the symptoms of adrenal insufficiency will show a sudden

outburst and be seen in all their intensity. Boinet has also laid stress on the appearance of serious accidents after excessive fatigue. Such occurrences confirm the investigations of Abelous and Langlois and of Albanèse upon the influence of fatigue on experimentally decapsulated animals.

Another theory accounts for the aggravating effect of intercurrent infections from the fact that, the antitoxic action of the adrenals against certain toxins no longer being exerted, the accidents due to intoxication are more severely manifested. It is evident that this hypothesis explains better than the former the phenomena of excitation, viz., delirium, convulsions, fever.

Sudden death, or at any rate death taking place within a few minutes, is not rare in the bronzed disease, and Addison had already referred to such a termination in his monograph. In 1896 Ihler was able to collect 18 cases, and since that time numerous instances have been noted. Certain cases of sudden death in apparently healthy persons have defied explanation until the autopsy disclosed a tuberculous or cancerous process of the adrenals.

The advent of death may be truly fulminating; a patient previously exhibiting no signs of aggravation in his condition may drop dead while getting out of bed or on attempting to lift a chair. The patient of Dupaigne-Béclère, who was among the first to be treated with relative success by opotherapy, died suddenly in bed during her convalescence. In some cases the end is marked by symptoms of a more striking character, such as a sudden attack of severe vomiting, convulsions, etc. The pulse becomes frequent and thready; the face cyanosed; dyspnea develops, and death occurs.

Accidental syncope, nervous shock, acute intoxication, and sudden adrenal insufficiency have all been advanced as hypotheses in explanation of such occurrences. It is difficult to believe, in this connection, that adrenal insufficiency can produce so rapid an effect since it is well known that completely decapsulated animals survive for fifteen to eighteen hours and show progressively increasing intensity before death. It appears to us more reasonable to attribute the termination to nervous shock originating in the adrenal or periadrenal sympathetic nerves, and reacting on the general organism with its cardiac and vascular inefficiency resulting from decreased tonic activity on the part of the adrenals.

Case of Addison's disease in a negress, aged 55 years. The face and backs of the hands and fingers were intensely black—much blacker in hue than other parts of the body. The palms of the hands were also abnormally pigmented, but to a lesser degree than the face. There were numerous irregularly defined areas of pigmentation on the mucous membrane of the cheek, gums, and tongue. Her pulse was frequent, small, and regular.

At the necropsy the vagina showed evidence of chronic inflammation of its mucous membrane and presented patches of pigmentation similar in character to those present in the mouth. On the vulva were a few small leucodermic areas. Both suprarenals were enlarged and exhibited caseous masses in their substance, apparently affecting the cortex. Their capsules were much thickened and adherent to the surrounding parts. They contained caseating masses, at the margin of which were giant cells, in the cortex. The condition was tubercular, with tendency to caseation. R. Seheult (Lancet, Aug. 3, 1907).

Three cases of Addisonism occurring in the same family, in sisters,

aged 9, 6, and 3½ years, respectively. The father, mother, and an elder sister, aged 19 years, were all healthy. The case of the girl aged 9 years was one of true Addison's disease. Croom (Lancet, Feb. 27, 1909).

Clinical Varieties.—Several forms of Addison's disease have been described according to the relative prominence of certain symptoms. These include the gastrointestinal form, painful form, melanodermic form, and asthenic form. These divisions are worthy of acceptance because they correspond in each case to a development and pathogenesis differing from the others. It seems probable, indeed, that in the melanodermic as well as in the painful form sympathetic changes predominate from the outset, while, in the asthenic form, adrenal insufficiency is the primary cause.

According to Finkelstein, of Paris, Addison's disease in infancy is not rare, occurring in sucklings as well as in later months. Most cases are due to tuberculosis of the adrenals, although some cases have been associated with the perfectly normal glands. The most important symptom is pigmentation of the skin, although pigmentation may be brought about by a long-continued diarrhea in infants. Other symptoms are general depression and extreme weakness, diarrhea and vomiting, and convulsions. The pulse is weak and irregular. The disease is always fatal, dissolution being due to weakness, or to some intercurrent disease, especially tuberculosis.

Addison's disease in children. Before puberty, *i.e.*, under 13 years, it presents considerable differences from that above this age, and is extremely rare. Analysis of 25 cases, including a personal one. As to relative frequency, Monti found among 200 cases 6 in children below 13, while Greenhow in 330 found it four times; in other words, 1 to 62.

Etiology.—The main etiological factor is tuberculosis, though the patient of Anglade and Jaquin showed no such lesion in the adrenal glands, although extensive tuberculosis in the lungs and spinal cord was present. Age: Twelve cases occurred between the ages of 10 and 13 years, 4 cases between 5 and 10, while 9 occurred below the age of 5. The youngest case on record is that of Belyayeff, of a child 7 days old. Contrary to what textbooks state, that the disease occurs far more frequently in boys than girls, the occurrence in males and females is about equal.

Family History.—Tuberculosis occurred as a family taint in 4 cases; in one instance a rheumatic history; in one instance the mother and four children had had the disease.

Previous History.—In 13 cases in which this was obtained there was tuberculosis of other organs in 3, measles in 2, scarlet fever in 2, tonsillitis and chorea in 1. Felberbaum and Fruchthandler (N. Y. Med. Jour., Aug. 10, 1907).

Hypoglycemia should be included among the symptoms of Addison's disease, as a corollary to the arterial subtension. Bernstein (Berl. klin. Woch., Oct. 2, 1911).

The writer found 6 cases on record in which the right suprarenal capsule was absent; in 2 Addison's disease developed, as the other suprarenal developed tuberculosis. He has recently seen a third case of aplasia of the right suprarenal. Schnyder (Schweizer med. Woch., July 14, 1921).

PATHOGENESIS. — The pathogenesis of Addison's disease cannot be explained except by referring to the data of physiology, and, while Addison was deserving of high credit for pointing out the relation of the bronzed disease to changes in the adrenals, the pathogenesis none the less remained obscure because the

functions themselves of the adrenals were still unknown.

Two important theories have been advanced, which, moreover, do not refer exclusively to lesions of the adrenals, but to which recourse is also had to explain the morbid syndromes related to lesions of all ductless glands, including the thyroid gland, the pancreas, etc. These are: 1. The nervous theory, which attempts to explain all the phenomena by an action of the nervous system through its adrenal connections. 2. The glandular theory, which attributes the disturbances to functional alterations in the adrenals.

Nervous Theory. — The nervous theory had already been clearly stated in Addison's second paper, which pointed out the close relations existing between the solar plexus, with the semilunar ganglia, and the adrenals. In France, Jaccoud became a strong partisan and defender of this theory. After him and after Addison, Habershon, Barlow, Schmidt, Mattei, and Martineau attributed the nervous disturbances observed to lesions of the solar plexus and semilunar ganglia. Following Jaccoud, this view is still held by Greenhow, Jurgens, von Kahlden, Lancereaux, Raymond, and Brault. These authors offer as arguments, on the one hand, changes in the adrenals in cases where during life the subject had exhibited none of the symptoms referable to Addison's disease and, on the other hand, the normal condition of the adrenals in individuals declared to have Addison's disease before the autopsy.

Jaccoud supported the theory on the basis of three orders of facts: the symptoms observed, the lesions found *post mortem*, and the structure of the adrenal glands. Among the symptoms observed, leaving the melanodermia out of consideration at once, the nervous disturbances are of two kinds: increasing asthenia and the gastric or nervous manifestations. Prof. Jaccoud, after referring to these symptoms, adds: "If we now bear in mind that in the uncomplicated cases these symptoms show progressive development in the absence of any important visceral lesion, without anemia, without albuminuria, without hemorrhage, and without diarrhea, they will without doubt appear to us as the direct and immediate result of a disturbance of the nervous system." We shall see later that these asthenic phenomena cannot be brought forth as arguments in favor of the nervous theory, and that the capsular theory, as conceived by Abelous and Langlois, itself finds strong support in the asthenia of Addison's disease, described by Jaccoud.

The autopsy in a case of Addison's disease in a child of 10 years showed tubercular infiltration of the lungs and enlargement of the bronchial glands. The suprarenal capsules were congested, but macroscopically they presented no lesions. A microscopic examination revealed no change in the histological structure. The capsule was of normal thickness, and the gland, as a whole, was not enlarged. The nuclei of the cells were distinct and there was no fatty degeneration. The semilunar plexus was somewhat altered and congested. The mesenteric glands were large, but not caseous. Upon examination the *Bacillus tuberculosis* was absent. Richon (Arch. de méd. des enfants, tome vi, No. 6, p. 350, 1903).

In every case of true Addison's disease there is a gray degeneration of the nerve-fibers of the splanchnics. This may be either protopathic, when one finds simple atrophy of the ad-

renals without other inflammatory appearances in these or other organs, or (more commonly) deuteropathic, in consequence of primary disease of the adrenals or pancreas. Withington (Med. News, Sept. 24, 1904).

Report of a typical case in which the lesions were located in the solar plexus, the suprarenals being free from tuberculosis. Laignel-Lavastine and Porak (Bull. de la Soc. Méd. des Hôpitaux, July 5, 1918).

The attacks of vomiting and the epigastric and lumbar pains are, indeed, in favor of nervous lesions, and it can readily be understood how the close proximity of the sympathetic nervous structures may explain the motor and sensory disturbances observed in cases of bronzed disease. As for the structure of the adrenals, it does not permit of our forming any definite opinion.

While it is quite true that these glands receive a large number of nerve-fibers from the sympathetic, as shown by the researches of Nagel, Bergmann, Kölliker, and Henle, there exist in the cortical layer ganglionic cells which may constitute reflex centers (Moers, Joesten, Holm); and while it is true that excitation of the adrenals tends to inhibit the intestinal movements (Jacob), yet the rôle of the adrenal bodies cannot be denied, even on the ground of their texture alone. The main argument against the pathogenetic rôle of the adrenals is based on the following double series of observed facts: Melanodermia may exist without lesions of the adrenals; marked lesions of the adrenals may exist without melanodermia.

Glandular Theory.—The researches of Brown-Séquard, which followed the monograph of Addison at an interval of but a few months, were steeped in the idea which then prevailed as to the "predominance of melanodermic disturbances in the bronzed disease." Furthermore, while unable to observe pigmentation of the skin in animals deprived of their adrenals, he pointed out the presence of numerous pigmentary granulations in the blood. The most prominent result of his researches, however, lay in the discovery of the functional importance of the adrenals, of which the rôle had until then escaped physiologists. "Death resulting from changes in these organs," wrote this author, "is preceded by a gradually developing weakness, going on to paralysis of the posterior extremities, then of the anterior, and finally of the respiratory muscles. Among the disorders noted may also be mentioned anorexia, failure of digestion, rather frequently delirium, epileptiform disturbances, and a gradual lowering of the temperature." Brown-Séquard concluded that destruction of the adrenals was followed by accumulation in the blood of a toxic substance having the property of becoming transformed into pigment. Since 1855 the investigations on the adrenals have been numerous. The conclusions of Brown-Séquard have been vigorously attacked. Philippeaux, Gratiolet, Harley, Berutti, and Martin-Magron combated the vital rôle of the adrenals, asserting, contrary to the belief of Brown-Séquard, that destruction of these organs did not necessarily result in death.

Tizzoni, in numerous researches carried out between the years 1884 and 1889, likewise recognizes the possibility of survival after destruction of both adrenals; but he points out at

the same time the possibility of regeneration of these organs when not totally destroyed; finally he referred to medullary disorders succeeding upon destruction of one adrenal.

Stirling showed that in a certain number of cases survival after destruction of both adrenals is explained by the presence of accessory adrenals. Alezais and Arnaud ascribed the fatal ending to ascending degeneration reaching the cord by way of the splanchnics.

> Clinical and autopsy findings in 3 cases: The morbid changes in the suprarenals were accompanied by corresponding changes in the other glands with an internal secretion, the thyroid, hypophysis, and spleen—all of these were hypertrophied, with evidence of hyperfunctioning. The writer does not regard Addison's disease as due to a single gland, but to several participating in the process. The first symptom in one patient was tremor of the arms, probably the result of professional exposure to electric currents, the man's work being done under an electric light of between 15,000 and 20,000 candlepower. The effect of the Roentgen rays on glandular organs suggests that the light here may have affected the cervical sympathetic, the thyroid, and the hypophysis. Later the process seems to have extended to the abdominal sympathetic and suprarenals. In another case atrophy of the ovaries followed a pregnancy with premature menopause. Calcareous degeneration of the thyroid followed, with tuberculous infection later and fulminating suprarenal symptoms. The diseased suprarenals could not obtain help from the ovaries and thyroid, and there was merely slight hyperfunctioning of the hypophysis as a defensive reaction. In the 3 cases patients in the last stages of Addison's disease recovered their energy and the bronzing subsided under thyroid treatment. The thyroid was already modified and was inadequate to supplant the diseased suprarenals, but it only required slight additional aid from without to be able to counteract temporarily the destructive process in the suprarenals. The disease, the course, the outcome, the histologic findings, the research in the experimental field, all sustain the assumption that Addison's disease, in its complete form, is a general affection of the entire great sympathetic system. Leonardi (Policlinico, Aug., 1909; Jour. Amer. Med. Assoc., Oct. 2, 1909).

In 1891, Abelous and Langlois published their first researches on the functions of the adrenals in frogs; these were followed by a series of papers on the functions of the glands in other animals. They showed that, in all animals subjected to double adrenalectomy, death promptly and inevitably occurs, but that a portion of an organ if left behind is sufficient to cause survival. Muscular weakness and asthenia are all the more intense if the animal be forced to perform muscular movements, whence their first conclusion "that the adrenals possess the function of neutralizing or destroying toxic substances evolved during muscular labor." This conception of the rôle of the adrenals explains a portion of the symptoms observed in Addison's disease, including the most characteristic symptoms: asthenia and the disastrous effects of fatigue.

The discovery of the vasoconstricting action of suprarenal extract by Oliver and Schäfer, on the one hand, and Cybulski, on the other, that of the presence of the active substance in the blood of the capsular vein (Cybulski and Langlois), that of the rapid destruction of this substance in the organism (Langlois), and finally

the isolation of adrenalin by Takamine also threw new light on the symptoms observed. The lowered vascular tension and the cerebral disorders can henceforth be interpreted as resulting from diminution of the tonic influence of the adrenals. The syndrome of adrenal insufficiency in its entirety can henceforth be explained through the data of experimental physiology.

Study of the nitrogen and sulphur metabolism in a patient who had Addison's disease and who was on a purin-free diet. The desamidating capacity of the patient (capacity to reduce amid nitrogen) and his capacity to transform the sulphur of the cystin group into sulphuric acid were absolutely comparable to that of normal individuals. A considerable degree of acidosis was observed, which is not accounted for by any factor which was found in this examination. The endogenous metabolism of the patient, as represented by the kreatinin and uric acid outputs, was below that of normal subjects. Wolf and Thacher (Arch. of Int. Med., June, 1909).

The writer, who had previously observed a striking hypoglycemia after removal of the adrenals, now reports the effect upon the glycogen content of the liver and muscles of the same procedure. Seven dogs were killed at intervals of four and one-half to eight hours after removal of the adrenals. At this time all showed great muscular weakness. Their livers contained an average of 0.722 per cent. glycogen. If one animal be excluded, the average of the other six was 0.222 per cent. Schöndorff found 18.69 to 7.3 per cent. of glycogen in the livers of normal dogs on a similar diet. The muscle content of glycogen was 0.653 per cent., compared with Schöndorff's average of 4 per cent. In three dogs dying spontaneously after operation, the livers contained no glycogen whatever, the muscles an average of 0.187 per cent. The lack of glycogen is the cause of the hypoglycemia. The muscular weakness is, in all probability, due to lack of sufficient sugar and sugar-producing material, for muscle glycogen is well known to be far less readily available for the body than is the liver glycogen. Porges (Zeit. f. klin. med., Bd. lxx, S. 243, 1910).

Adrenalin glycosuria is due to the conversion of liver glycogen into sugar. In animals rendered glycogen-free by starvation and strychnine poisoning, adrenalin injections cause a new formation of glycogen and sugar. Pollack (Arch. f. exper. Path. u. Pharmak., Bd. lxi, S. 149, 1909).

Even the insufficiency or complete failure of adrenal opotherapy finds its explanation in the instability of suprarenal extracts. (We retain this vague term to convey the fact that adrenalin is but one of the principles now isolated which are elaborated by the adrenals).

But while physiology can explain and experimentally reproduce most of the symptoms of Addison's disease —those which Bernard and Sergent classify in the syndrome of pure adrenal insufficiency—she has shown herself entirely powerless to reproduce and explain the pigmentation which is so characteristic of this affection.

Excepting in one observation by Boinet, no experimenter has been able to produce pigmentation experimentally, either by destroying the adrenals or by setting up local irritation.

Following Loeper we shall refer into four groups the theories which have been advanced to explain melanodermia: adrenal origin, cachectic origin, nervous origin, and mixed glandular and sympathetic origin.

A. Adrenal Origin.—The elaboration of a pigment by the secretion of

the adrenals, thought of by Brown-Séquard and Pfandler, and which would be caused by lesions of the organ itself, is not supported by any evidence of value. The hemolytic function of the gland and the accumulation in the blood of pigment derived from hemoglobin when the glandular function is weakened are likewise too hypothetical.

B. *Cachectic Origin* (Gubler, Teissier, Debove).—It is certainly true that any cachexia may provoke, along with general nutritional disorders, pigmentary phenomena. But the bronzed disease is frequently manifest previous to the establishment of cachexia, and presenting features which give it a specific character which does not bear well with the general processes of the cachexia.

C. *Nervous Origin.*—The intimate connections existing between the adrenals and the sympathetic system are such as to warrant a belief in functional changes in this system during Addison's disease. Addison had already thought of the possible rôle of the nervous system. Jaccoud, Lancereaux, and Raymond defended this theory.

The clinical observations of Semmola and of Brault, who noted melanoderma in conjunction with simple compression of the semilunar ganglia and solar plexus, and the cases of Addison's disease with lesions of but one adrenal (Greenhow) are cited as favoring the view of nervous origin. Irritation of the sympathetic would presumably bring about an overproduction of pigments, either in the blood itself (von Kahlden, Nothnagel), in the chromoblasts (Raymond) or in the cells of the epidermis (Béhier, Chatelin).

D. *Mixed Origin.*—Attractive as the nervous theory may be, it does not suffice in all cases, and especially is in complete disagreement with experimental facts, since all excitations of the sympathetic, whether extra- or intra- capsular, have proven without effect in producing melanodermia. A number of physicians are at present adopting the opinion of Loeper, that melanodermia is the result of changes both in the adrenals and the nervous network surrounding them. According to Loeper, the adrenal secretion is the normal and necessary exciting agent of the nervous system in its function of regulating pigmentation. Sajous (1903) and Laignel-Lavastine hold an opposite view: the sympathetic is not the regulator of pigmentogenesis, but of the adrenal gland itself, on which the formation of pigment depends.

Two cases, pronounced hypoplasia of the chromaffin system, accompanied the typical Addison's disease, while the lymph-glands were enlarged. V. Werdt (Berl. klin. Woch., Dec. 26, 1910).

Case of chronic Addison's disease in a youth with the thymolymphatic temperament. The suprarenals had been totally destroyed by a primary tuberculous process, as also in a similar case in a man of 41 with the status lymphaticus. Analysis of these cases and of similar ones in the literature seems to demonstrate a mutual stimulating action between the thyroid and the suprarenals and between the thyroid and the thymus, while there is mutual inhibiting action between the suprarenals and the thymus. Kahn (Virchow's Archiv, June, 1910).

Case of male fern poisoning in latent Addison's disease. The remedy was given with castor oil for a tape-worm. The autopsy showed tuberculosis of the adrenals—a true Addison's disease. Most of the cases

of poisoning by male fern are those in which employment of the drug has been followed by the administration of castor oil. The use of the combination is strongly warned against. F. Schotten (Münch. med. Woch., Nov. 3, 1914).

[I have long urged that the adrenals took part in the autoprotective functions of the body, and that when they were diseased poisoning occurs more readily. Hence also the vulnerability of such cases to infection. C. E. DE M. S.]

DIAGNOSIS.—The various symptoms encountered in Addison's disease may be divided into two groups:

A. Symptoms of adrenal insufficiency.
Cardiovascular disturbances:—
    Lowered arterial tension. Tachycardia.
    White line on abdomen.
    Cerebral anemia. Syncope.

Disturbances of metabolism:—
    Lowered temperature and sensation of cold.
    Progressive asthenia. Wasting. Prostration.
    Encephalopathy and various nervous disorders. Vomiting and diarrhea.

B. Symptoms of irritation of the adrenal sympathetic.
    Melanodermia.
    Radiating pains.
    Vomiting and diarrhea.

Where the Addisonian syndrome is complete and the course rapid, the diagnosis is easily made. It becomes more difficult when melanodermia is absent or doubtful. A study of the resistance to fatigue, either by means of the ergograph or by simply causing the patient to perform a definite piece of work, combined with the use of the sphygmomanometer, may be of value in facilitating diagnosis, but very often in the hospital, in cachectic tuberculous subjects, the involvement of the adrenals is not discovered till the autopsy.

In fact, the question of diagnosis is generally raised when it becomes necessary to attribute the melanodermic patches to Addison's disease or, on the other hand, to some other affection producing pigmentary changes, such as the pigmentation of cachectic tuberculous cases, pigmentation of hepatic origin, the melanodermias of malaria, arsenic poisoning, lead poisoning, and phthiriasis.

The most common fallacy is to mistake Addison's disease for pernicious anemia; the peculiar lemon tint of the skin in the latter condition, however, is different from that of the characteristic case of Addison's disease; but in slight cases confusion often arises. Fortunately, modern means of examination of the blood, which in Addison's disease is but little abnormal, enable the recognition of the marked blood characteristics of pernicious anemia.

The writer, however, advises caution against being content with negativing a diagnosis of pernicious anemia because a single blood examination fails to show characteristic changes. The blood in pernicious anemia varies from day to day and from hour to hour.

Another possible source of confusion commonly met with, is the discoloration consequent on prolonged administration of arsenic. By inquiry of many persons of considerable experience in arsenical poisoning the writer finds that the occurrence of pigmentation in the mouth is in favor of the case being Addison's disease. In malignant disease the wasting is apt to be much more marked, and local evidence of malignancy can usually be found.

Other pathological conditions sometimes confounded with Addison's disease, but which ought to be easily distinguishable, are the filthy, dirty patients, infested with lice, sometimes seen in hospital out-patient departments; phthisical and syphilitic pig-

mentation; Hanot's cirrhosis of the liver, and bronzed diabetes.

Any condition that destroys the functional activity of the medullary part of the suprarenals may cause Addison's disease, by far the most common being tuberculous degeneration. Calmette's reaction helps in this matter. The comparative frequency of malignant disease as a cause, the author considers due to the necessity of having both suprarenals affected, and, perhaps, to the fact that in malignant disease death will be occasioned before the evolution of characteristic phenomena. The proportion of cases in which clinically characteristic Addison's disease has failed to show disease of the suprarenals is so small, about 12 per cent., as to be within the margin of allowable error due to erroneous diagnosis, inefficient post-mortem examination, or the possibility of functional disturbance of the suprarenals. Further, other glands, e.g., the internal carotid and the coccygeal, have cells functionally resembling those of the suprarenals, and it is conceivable that very rarely disease of these glands may cause Addison's disease and lead to death before the suprarenals are affected. On the other hand, when the suprarenals have been found to be diseased, and yet no Addison's disease has been present, it may be that the vicarious activity of these other glands may have formed sufficient internal secretion to prevent the patient having Addison's disease. W. H. White (Clinical Journal, Mar. 18, 1908).

The melanodermia of phthisical patients is all the more likely to lead one astray because of the fact that the cases of Addison's disease are almost all tuberculous. For some authors, moreover, the majority of melanodermic tuberculous cases are cases of Addison's disease in which the adrenal changes are just beginning, not yet showing the signs of glandular insufficiency, but having

pericapsular lesions which cause a precocious melanodermia. In pigmented tuberculous subjects without Addison's disease the pigmentation is said to be of a lighter grade and especially the mucous membranes to be unaffected.

Three cases of tuberculosis of the suprarenals in which there was no pigmentation. The diagnosis was made in two from the remarkable weakness of the patients in strong contrast to their well-nourished aspect. Another sign is the low blood-pressure, not to be explained to any disturbances on the part of the heart. Gastrointestinal disturbances without traceable cause are further corroborative testimony. These findings differentiate Addison's disease even without pigmentation of skin or mucosæ. Stursberg (Münch. med. Woch., Bd. liv, Nu. 16, 1907).

Cases of liver cirrhosis and even a few incipient hepatic cases without appreciable change in the size of the liver present either disseminated hepatic patches of discoloration or a diffuse melanodermia of the same color as in Addison's disease. Here again the mucosæ are but slightly or not at all involved, and the hepatic disorders place one on the right track.

Arsenical pigmentation is a rare occurrence; the same is true of saturnine pigmentation. In the latter the blue line on the gums is generally sufficient to permit diagnosis. In pigmentation due to arsenic, the color is more slaty in hue, and a dark mottling is also present, which is rather characteristic. Finally the signs of arsenical intoxication, together with the absence of those of adrenal insufficiency, serve to establish the diagnosis.

In malarial subjects the pigmentation again does not involve the mu-

cous membranes, it is more diffuse and uniform, and the special indications of malaria are present.

The melanodermias of phthiriasic origin (pediculosis) seen among vagabonds in a state of physiological debility, and who are bearers of parasites, are accompanied by itching and cutaneous excoriations. The causative agent may be discovered.

On the whole, it should be borne in mind that the melanodermia of Addison's disease differs from other forms of pigmentation in that it shows marked preference for mucous membranes, although this characteristic should not be put down as absolutely distinctive.

> Early diagnosis is all important, though often very difficult. The disease gives rise to definite signs and symptoms, and usually to marked lesions of the medulla of the suprarenal gland. The solar plexus is frequently diseased, owing to the influence of the secretion of the gland in stimulating the sympathetic system. Pathognomonic signs are asthenia, pigmentation, vomiting, and attacks of faintness. If these symptoms are well marked the diagnosis is not difficult, but when they have become evident the chances of successful treatment are not good. Grunbaum (Practitioner, Aug., 1907).

> Two personal cases which emphasize the resemblance existing between Addison's disease and tabes dorsalis. Both patients presented an almost identical pigmentation, and both had muscular atrophy. One was a typical case of Addison's disease, while the presence of tabes was undoubted in the other. It is not necessary to assume a combination of tabes dorsalis with Addison's disease, however, since other symptoms of the last-named affection were lacking. The pigmentation should rather be referred to tabetic changes of the nervous system. Possibly the pigmentation in

> Addison's disease is likewise the expression of disease on the part of the nervous system. In this particular instance atrophy of the shoulder muscles was said to have been present ever since birth, and atrophy of the thigh muscles was claimed to have followed later, in connection with traumatism. Wagner (Berl. klin. Woch., Nu. 15, 1908).

TREATMENT. — Addison's disease of pure type or manifested in the syndrome of adrenal insufficiency without melanodermia is largely caused by tuberculosis of the adrenals. The general treatment of tuberculosis, or rather that form of treatment which is in vogue in a given locality at the time, is indicated. Syphilis of the adrenals is rarely diagnosticated during life; at the autopsy may be found either extensive gummata, a miliary syphilosis or, especially in the young, a sclerosis resulting in atrophy of the gland. In doubtful cases the effect of specific treatment may be tried. Certain cases seem to have been benefited by the **iodides,** with or without the addition of **mercury** (Schwytzer, A. Andrews).

Cases of *bona fide* acute adrenitis with or without hemorrhage, which are almost always frankly infectious in origin (small-pox, diphtheria, etc.), generally run a very rapid course and do not possess any special line of treatment. As for the morbid growths—sarcoma, epithelioma, carcinoma, etc.—which it is almost impossible to diagnosticate during life, unless perhaps it be when persistent edema is noted in combination with the usual syndrome, surgical intervention is indicated, though the results obtained by Israel, Mayo, Kelly, Lecenne, and Hart-

mann have afforded but little encouragement.

Physiological data naturally led to the trial of **adrenal opotherapy**. This treatment was first instituted by Abelous, Charrin, and Langlois in the form of a glycerin extract of the adrenals of guinea-pigs, dogs, and horses. The patients were in such a state of cachexia that no results were obtained, but in two less advanced cases, employing injections each representing Gm. 0.10 of the dried extract, Langlois obtained better results and in particular a notable diminution of the asthenia.

Since that time numerous trials have been made and the treatment markedly altered. Among the methods that have been tried are: 1. Hypodermic injections of the extract. 2. Ingestion of fresh or dried glandular substance. 3. Injection of adrenalin solution. 4. Grafting of adrenal tissue.

1. The injections of extract of the suprarenals were early abandoned because of the great pain they occasioned and the fact that they failed to give satisfactory results in a large number of cases.

2. The ingestion of fresh or dried gland has furnished a few unhoped-for results, together with numerous failures. Béclère and Andérodias report cases of cure, or, perhaps better, disappearance and long-continued absence of the symptoms of adrenal insufficiency. It is advised to use the adrenals of calves and start with doses of Gm. 1.5 to 2.0, which are gradually increased to Gm. 6.0. Sajous employs the dried gland (the glandulæ suprarenales siccæ of the U. S. P.). The dried extract may be given in capsules in the dose of Gm.

0.25 to 0.35 daily for ten successive days; it is left off for four days, then resumed for six to eight days, etc. Systematic testing with the sphygmomanometer should be used as a guide in the treatment. Improvement in the arterial tone is to be considered the sign of efficiency in the treatment, while any indication of hypertonicity demands immediate stoppage of the administration of adrenal.

Adams's paper in the Practitioner for October, 1903, includes an analysis of 97 cases treated with a preparation of the **suprarenal glands.** Of these, 7 were distinctly made worse by the treatment, 43 derived no benefit, 31 showed marked improvement, and 16 were cured.

The methods in the use of glands in these cases may be divided into five heads: 1. Suprarenal grafts. Three patients were treated by this method and all died. 2. Nine patients were treated by fresh glands given by the mouth; of these, 1 became worse, 1 was not benefited, 6 were improved, and 1 permanently relieved. 3. Eleven patients were treated by hypodermic and intramuscular injection. One became worse, 6 derived no benefit, 3 were improved, and 1 permanently benefited. 4. Sixty-one cases were treated with the fluid or solid extract of the suprarenal gland by the mouth. Of these, 2 were made worse, 32 derived no benefit, 17 were markedly improved, and 10 were permanently relieved. 5. Five patients were treated by mixed methods; 3 were improved and 2 cured.

The cases most likely to derive benefit from the specific treatment are those in which the process is a chronic sclerosis and in which the other organs are fairly sound. D. Symmers (Med. News, Sept. 10, 1904).

Series of 120 cases collected from literature, including 97 previously collected by E. W. Adams, in all of which **adrenal preparations** had been used in some form, gave the following results:

Analysis of these cases shows that far better results could be obtained by a careful adjustment of the dosage to the actual needs of each individual case. Addison's disease being due, from the writer's viewpoint, to inadequate oxygenation and metabolic activity, the result in turn of a deficient production of the adrenal secretion, it follows that *the temperature and blood-pressure indicate the degree to which the adrenals are still performing their functions.* It is plain, therefore, that our aim should be *to supply only just enough adrenal extractive to compensate for the deficiency of adrenal secretion produced.*

The 25 cases of Addison's disease in which, out of the 120 referred to above, permanent benefit occurred include one, treated by Bate, in which but $\frac{1}{12}$ grain (0.005 Gm.) of **adrenal extract** three times daily caused very great and lasting improvement with marked lessening of the bronzing. When the remedy could not be obtained temporarily, which occurred twice, the case relapsed. On the other hand, Suckling began with 10 grains daily and gradually increased until 175 grains were given each day, and also obtained favorable results. That in Bate's case the adrenals were still able almost to carry on their function is self-evident, while in Suckling's the remedy practically compensated for the adrenals (while the local morbid process in them was still active, and such as to paralyze their functions—a fact well shown by the severity of the case when the use of the extract was begun). The average dose is probably that used by Weigall in a very severe case—5 grains, increased to 10 grains, of the extract three times a day. The patient increased 6 pounds in two

weeks, and after about three months 56 pounds. In other words, in the 25 cases of permanent benefit, although the remedy was used empirically, it so happened in all probability that *the doses employed coincided with the needs of the organism.* In the 51 cases in which no benefit was obtained several occur in which failure was evidently due to inadequate dosage or to too early cessation of the treatment, while in others excessive doses—practically in every instance a too rapid or excessive increase of the dose—as clearly prevented a successful issue. Sajous (Monthly Cyclo., April, 1909).

3. The injection of **adrenalin** recommended by Netter and Sergent appears to us best suited for the cases showing low arterial tension, whether of adrenal origin or not.

4. **Grafting of adrenal tissue.** The only rational treatment for adrenal insufficiency is grafting of the gland. Experimentation shows, indeed, that the substances secreted by the gland are very quickly destroyed in the organism, and that either the ingestion or injection of the extract can, therefore, produce but very evanescent effects, which, besides, cannot completely replace the activities as yet unknown having their seat in the glandular cells themselves. Unfortunately, success in adrenal grafting is not easily obtained, and in cases where the vitality of the grafted gland has manifested itself accidents of so grave a nature have been noted that grafting has been considered an impracticable method. Courmont reports 3 cases of the grafting of dogs' adrenals in man and states that in all of them the results were disastrous. His personal case developed a formidable hyperthermia and cardiac collapse.

Sajous has collected from the gen-

eral literature 120 cases of Addison's disease treated by opotherapy in its various forms and presents the following table:—

1. Cases in which death can be ascribed to grafting or adrenal preparations . 8
2. Cases in which benefit was slight or nil 51
3. Cases in which marked improvement occurred 36
4. Cases in which permanent benefit was obtained 25

120

In a typical case reported by the writer in a woman of 35 years, **adrenal gland, tuberculin** every 10 days, and **iron** and **arsenic,** caused improvement, the blood-pressure rising from 95 to 110. In 6 weeks the patient was very well, and went to the country. She soon relapsed, however, and the treatment was repeated with no good effect. During a period in which she was very weak and low, **transplantation of an adrenal** was performed. On March 17th a male patient died of heart disease. The cadaver was taken immediately to the anesthetising room adjoining the operating theater, and the right adrenal removed and placed in normal saline solution at 100° F. In the operating theater cocaine and adrenalin solution was infiltrated over the lower ends of the patient's recti abdominis. A longitudinal incision was made on each side, and the sheaths of both right and left recti laid open. The adrenal was bisected, and half of the gland was then buried in each rectus muscle. The sheaths of the recti were then closed with continuous catgut sutures, and the skin wounds with horse hair. The patient was very ill after the operation, but from 21st March improved rapidly. By 2d April she was up, and was at the time of writing in comparatively good health. The pigmentation was distinctly less, and she had gained one stone (14 pounds) in weight. The blood-pressure on the 19th June was 104. D. Murray Morton (Austral. Med. Jour., July 6, 1912).

In a typical case of Addison's disease observed by the writer, the patient's weight had come down from 186 to 95 pounds. None of the remedial measures used were of the least avail. He was then placed upon fresh **adrenal glands** from the sheep, taking them raw and minced. As he developed repugnance to these desiccated gland was substituted. The improvement was striking, all the symptoms showing change for the better. He had recovered 50 pounds of his weight, and his improvement otherwise was harmonious, when suddenly and without apparent cause acute gastritis set in, with prostration. It was found that he had suspended his adrenal treatment for over 3 weeks. His stomach was unable to retain anything. Cerebral symptoms now set in and death took place from coma. The lesson of this case is that we have not sufficiently tested organotherapy in these cases. Klein (Deut. med. Woch., Aug. 1-8, 1912).

True Addison's disease can often be benefited, and sometimes even recovered from, at least in its glandular manifestations (its most important ones) by **adrenal opotherapy,** which not only makes up for deficiency of secretion, but also leads to a compensatory hypertrophy which to some extent replaces lost glandular tissue. Sergent (Jour. de Méd. et de Chir. Prat., June 10, 1913).

A typical case of Addison's disease in 1902, cured with **adrenal gland,** left as only symptom a discrete melanodermia. Eleven years later the patient died of gastric cancer. The autopsy showed a small cicatrix in the left adrenal. Hirtz and Debré (Paris Méd., June 27, 1914).

In a case of advanced Addison's disease observed by the writer, an intravenous injection of adrenalin caused sweating over the entire body and then sudden arrest of both the heart and the respiration. Only after half an hour's vigorous artificial respiration was the patient revived. In another case an intravenous injec-

tion was followed by intense tremor and pallor, and the left side of the face alone was bedewed with sweat. Lowry (Med. Klinik, Nov. 1, 1914).

Exceptional cases as regards the extreme tolerance of the patient for **epinephrin.** The man of 38 with grave symptoms of suprarenal insufficiency was given 10.5 mg. (¼ grain) epinephrin in four and a half hours; this included 2 mg. (½₂ grain) subcutaneously and 8.5 mg. (⅛ grain) intravenously. No sugar appeared in the urine and the blood-pressure was not brought up quite to the normal figure even with this. The following days 6 and 4 mg. (1/10 and 1/16 grain) were given. There were no signs of intolerance at any time, even though to attain the desired therapeutic result these large doses were found necessary. The case teaches that we need not shrink from large doses of epinephrin in emergencies, as with acute suprarenal insufficiency under chloroform, or with gaseous gangrene or other hypotony of infectious origin. By watching over the blood-pressure as the epinephrin is being taken, we can continue it and push it until the arterial pressure is brought up to a point where the functioning of the organs is possible once more. Nolf and Fredericq (Arch. Med. Belges, Aug., 1917).

Two cases treated by the writer retrogressed even to the pigmentation of the mucous membranes under tonics and systematic administration of **suprarenal gland.** The patients were men of 65 and 70 who had been subjected to great privations. The suprarenal deficiency had evidently been merely functional. Quincke (Therap. Halbmonatshefte, Jan. 15, 1920).

If tuberculosis is suspected the treatment of this condition should also, according to Sajous, be resorted to.

In a case observed by the writer suspected of tuberculous origin, the patient's sister having died of tuberculosis, the patient was treated in the usual climatic and general hygienic way, and in addition received several courses of **tuberculin** injections. The patient is in good health and able to perform rather arduous duties. Munro (Brit. Med. Jour., Mar. 23, 1912).

[The administration of adrenal gland alone often fails to cure. In truth, adrenal gland should be regarded only as an important adjunct to the treatment of the causative disorder, and an agency calculated to compensate for the reduced secretion the diseased adrenals produce. C. E. DE M. S.]

J. P. LANGLOIS,
Paris.

ADENTIIS. —DEFINITION.—
Inflammation of a gland.

VARIETIES.—Adenitis may be *acute,* due almost invariably to infection from an attack of angioleucitis and occasionally to injury or strains; or *chronic,* resulting from either of the preceding, especially in strumous or cachectic persons, and from slight sources of irritation, and not uncommonly resulting in permanent enlargement and induration or in tuberculous degeneration. Adenitis of specific origin will be described under SYPHILIS and URINARY SYSTEM.

ACUTE ADENITIS.

SYMPTOMS.—The general symptoms depend upon the extent and severity of the infection. Rigors may occur when pus forms. The temperature is frequently elevated. If the infection is severe, symptoms of profound septicemia appear.

The local symptoms are, by far, the most prominent in the majority of cases, and consist of pain, heat, and swelling. The suffering varies from a slight soreness only to intense pain according to the position of the gland, its relations with the surrounding tissues, and the

density of the tissue in which it is imbedded. The heat may vary according to the degree of the congestion present. The swelling may either be great or slight. If the lesion be confined to the gland, it will be well defined; if periadenitis is present, the swelling will be more or less diffuse. Glands in any region of the body may be affected, but those of the neck, axilla, and groin more than the others; this is due to the fact that infection generally enters the system through the mouth, throat, genital organs, and the extremities.

In the congestive, or exudative, stage, pain and swelling are present in the region of the glands; if the glands are superficial the swelling is ovoid, with the long axis coinciding with the direction of the afferent lymphatics, and palpation reveals several movable, hard, elastic, and tender rounded masses.

When the glands are deep, as in the axilla, abdomen, or even the neck, the results of palpation are less definite and unsatisfactory.

In the suppurative stage the pain increases and becomes sharp and catching, the skin reddens, and the periglandular tissue swells.

If the gland alone suppurates, the skin remains normal, while under it may be felt the softened and enlarged gland. This latter opens outwardly or into the neighboring cellular tissue on from the sixth to the fifteenth day of the affection. When the gland opens outwardly, the cicatrix is much smaller than when it ruptures into the cellular tissue, as in the latter case it gives rise to an abscess.

If the cellular tissue around the gland suppurates, the skin becomes quite hot, swollen, and painful, and fluctuation may be felt. Two foci of suppuration are thus established. The skin

is occasionally undermined by the pus. Recovery is possible, however, without suppuration of the gland.

Both the gland and the cellular tissue around it may suppurate, either simultaneously, or suppuration of the cellular tissue may precede that of the glands, or the latter may suppurate and rupture into the surrounding cellular tissue and form an abscess. Pus is usually produced in considerable quantity, and the affection is of long duration.

Suppurative adenitis may result in cicatrization after several weeks. This cicatrix may reopen to allow the exit of pus from a suppurated gland. On the other hand, a fistula may result, which may give exit to seropus or to lymph (Després). A lymphatic gland or vessel will then be found at the bottom of the abscess cavity, below the crater-like opening.

As the suppuration usually starts in more than one focus in the gland, the first sensation to the touch will be one of bogginess, which periglandular congestion may render obscure. Well-defined fluctuation is found only when considerable tissue is destroyed.

Two cases of adenitis of the elbow due to fever were observed by the writer. In the one case staphylococci were found in the pus evacuated from the epitrochlear lymph-node in a convalescing young child. The germs may have entered by a small wound of the thumb. In the second case of the same kind the epitrochlear lymphadenitis subsided without suppuration under systematic application of wet compresses. It was probably a primary typhoid lesion. L. Verdelet (Jour. de Méd. de Bordeaux, Apr. 21, 1912).

DIAGNOSIS.—The diagnosis of ordinary superficial acute adenitis is usually easy; it is more difficult when the neighboring cellular tissue is also

inflamed; it may be impossible in cases of deep-seated or visceral adenitis.

In adenitis of the inguinocrural region the swelling is found in the external portion of the region if due to a lesion of the gluteal tissues, and in the inner portion of the region if due to a lesion of the anus, perineum, or external genitals. In both conditions the tumor will have its long axis directed more or less horizontally.

The swelling will be found in the lower portion of the inguinocrural region, with the long axis directed more or less vertically, if the lesion causing it is situated on the foot, leg, or lower part of the thigh. This disposition is due to the anatomical relations of the lymphatic vessels and glands, and should be borne in mind. Operation for strangulated crural (femoral) hernia has been performed for an adenophlegmon of the crural canal.

> Supraclavicular adenitis, while frequent in phthisis, is not present in every case. Yet it is of great diagnostic value when present. There may be a few or a great number of slightly enlarged glands, and they are frequently bilateral. The cervical glands may also be enlarged. There is no pain, nor does the swelling increase, remaining just the same for years. They rarely accompany apical tuberculosis, but are generally found with peripheral, subpleural lesions. The writer considers that the presence of enlarged supraclavicular glands confirms the diagnosis of doubtful phthisis. C. Sabourin (Jour. des praticiens, Dec. 27, 1902).

> New sign described, based on auscultation at level of seventh cervical or first dorsal vertebra. When the child speaks in a low voice the voice sound is accompanied by an added whispering sound, localized to one or two vertebræ, or extending even to fourth or fifth dorsal vertebra. It is present long before dullness appears. The bronchial quality of respiration over this area is also significant, but it only appears when the glands are considerably enlarged. The absence of abnormal breath sounds and apical râles affords corroborative evidence. D'Espine (Brit. Med. Jour., Oct. 15, 1910).

ETIOLOGY.—The lymphatic glands serve as reservoirs on the course of the lymphatic vessels, through which any irritants or infection must pass.

> Glandular enlargement indicates an infective process situated in the lymph tissue specifically drained by such glands. In most cases of acute associated infection the glandular enlargement subsides as soon as the infective process is removed. When chronic cervical glandular enlargement persists in spite of local treatment of the throat the lymph tissue involved—the tonsils—is frequently the seat of a tuberculous lesion, the glands being secondarily infected. E. B. Gunson (Brit. Jour. Child. Dis., Oct.-Dec., 1917).

Cold and overexertion act as local depressants, and thus may indirectly favor the development of adenitis. General debility has the same effect. The following varieties of adenitis, etiologically regarded, are recognized:—

1. Adenitis by contiguity, resulting from the propagation, by contact, of a neighboring inflammation.

2. Adenitis by continuity or following lymphangitis.

3. Adenitis by embolism, due to the transportation of septic or irritating matter, produced in the system or coming from the outside.

Adenitis of the mesenteric glands may be due to dysentery or to the inflammation of Peyer's patches in typhoid fever.

Adenitis occurs in carbuncle, furuncle, vaccination, erysipelas, and eruptive or infectious fevers.

Attention has been called by many

observers to the frequent association of enlargement of the cervical glands and diseased tonsils. So often has this been found that every patient suffering from cervical adenitis should have the tonsils examined, with a view to their removal if diseased. The contents of the tonsillar crypts should be examined microscopically, and the identity of the bacterial growths therein ascertained. It is wise to submit the tonsillar mass to bactericidal measures—*e.g.,* **iodine in glycerin**—some time before removing them.

> The writer made histological examinations of 65 whole tonsils removed from children; 57 tonsils of patients not clinically tuberculous showed no tuberculous lesions. Of eight patients with tuberculous cervical adenitis the tonsils were found tuberculous in 5. F. S. Matthews (Annals of Surg., Dec., 1910).
>
> A child with enlarged tonsils and adenoids is not ill because of the increased size, but because of a chronic infection of its faucial and post-nasal lymphoid tissue, which serves not only as a nidus for the manufacture of toxins, but also as a port of entry for many other systemic diseases. This condition of chronic infection, which is extremely common, is easy to diagnose if the 3 cardinal physical signs—enlarged tonsils, rhinitis, and enlarged cervical glands—are kept in mind. Running ears, bronchitis, mastoiditis, etc., are physical signs to be noted, more correctly described as complications. The disease is highly infectious, as shown by the facts: (1) That it is far more frequent among school children than among children who do not go to school; (2) that when one child in a family is attacked the disease subsequently spreads to others who were previously healthy; (3) micro-organisms can always be grown from the nasal and post-nasal secretions, which are normally sterile. There is a tendency to chronicity, the child in such case

> being a "carrier" and consequently a source of danger to other children. P. W. Leathart (Brit. Med. Jour., Feb. 14, 1920).

PATHOLOGY.—If suppuration does not occur, resolution may take place, or chronic enlargement of the gland may follow hyperplasia of the connective-tissue stroma of the gland.

If suppuration does occur the surrounding connective tissue may, and usually does, suppurate; then the more or less disintegrated gland lies in a suppurating cavity formed by the circumjacent connective tissue.

There are two forms of acute adenitis, depending upon the degree of inflammation present:—

1. Exudative adenitis. In this form the gland is swollen, and it feels hard and elastic. On section it appears reddish brown, like the spleen, with small foci of hemorrhage, all of which indicate excessive dilatation of the capillaries. The lymphatic stream is arrested by the dilatation of the cortical lymph-sinuses and their obstruction by fibrin, granular material, and portions of altered white corpuscles. The lymph-follicles are filled with fibrin and accumulated lymph-cells. The stroma of the gland is swollen and infiltrated with cells.

If the section of the gland is scraped, a milky liquid will be obtained, which contains white corpuscles and epithelial cells, the latter showing several nuclei.

2. Suppurative adenitis. In this variety the gland softens, its tissues become more brittle, hemorrhagic infiltration centers form that soon change into yellow, purulent foci. These, at first distinctly separate, soon unite, forming an abscess within the fibrous capsule of the gland. Sometimes the

periglandular tissue suppurates, while the gland does not.

The glandular abscess and the periglandular abscess may open externally, each one separately or both simultaneously. The suppurating gland may rupture into the cellular tissue. Occasionally the gland is hard and elastic; it may be difficult to separate it from its fibrous capsule. The afferent lymphatics are enlarged and thickened. The lymph-cells and cortical follicles are few in number and have undergone granulofatty degeneration.

PROGNOSIS.—The prognosis is usually favorable; it may be unfavorable, however, when extensive abscesses form in the neighborhood of important organs.

Deep-seated suppurative adenitis may give rise to dangerous complications, especially in certain regions, like the neck and mediastinum, on account of the purulent extensions (through burrowing) and the difficulty of evacuating the pus.

Ulceration of the great vessels of the neck giving rise to grave hemorrhages may also occur.

TREATMENT.—The first indication in acute adenitis is to remove any source of irritation or infection. Any wound, abrasion, opening, or any natural cavity with which either of these may connect should be so treated as to bring about absolute local asepsis.

> Enlarged glands of the neck are not, primarily, tubercular, and bear the slightest relation, if any, to general or pulmonary tuberculosis. They are due to a mixed infection of pus-producing bacilli, and will quickly resolve if the source of the infection is removed before the glandular tissue becomes disorganized. If disorganization takes place, the gland should be poulticed until it is practically liquefied. It should then be opened by a stab puncture, emp-

tied and drained by a Briggs cannula. Cases seen late with a large mass of partially calcified and partially disorganized glands present call for a thorough and extensive dissection. Treatment, other than local, should be food, fresh air, and proper clothing. F. D. Donoghue (Boston Med. and Surg. Jour., Mar. 28, 1907).

The region in which the affected gland is situated should be kept at rest and, if possible, elevated. In this manner the afferent arterial current is diminished, while the efferent venous and lymphatic currents are increased.

To prevent suppuration, gray mercurial ointment, very gently rubbed in, is useful. The injections of from 5 to 10 minims of a 3 per cent. carbolic acid solution into an inflamed gland have also proven satisfactory.

If it is desired to hasten suppuration, warm antiseptic fomentations are to be used in preference to poultices. The compound resin cerate of the pharmacopœia is effective for this purpose, and is antiseptic as well.

When pus has formed, the gland should be opened by a generous incision, sinuses, if present, being opened throughout their entire length to facilitate treatment. The contents are then carefully removed, and the infiltrated wall scraped with a sharp curette. The cavity should then be packed with iodoform gauze, or gauze impregnated with camphorated naphthol or salol. The dressing may be removed on the third day.

> In addition to climatic and general tonic treatment, the writer advised the evacuation by puncture of suppurative adenitis and the injection of a mixture of iodoform, 1 part; ether, 10 parts; oil of sweet almonds, 100 parts; creosote, 2 parts. In chronic cases cure may be obtained in two or three months after about twenty punctures. Robin (Tribune méd., xli, 249, 1908).

Balsam of Peru is a valuable curative agent, as it is not only antiseptic, but is a stimulant to healthy granulation. It is applied directly to the open, cleansed wound, and then covered with gauze and retaining bandage.

In the treatment of cases of simple chronic adenitis, applications of **iodine, compression,** and **local blistering** have given the best results.

Blisters, **nitrate of silver,** or iodine tincture should be applied around, but not over, the inflamed gland.

Excision may be performed if the mass be large or disfiguring.

In cervical adenitis due to tonsillar infection some authors have strongly advised the thorough **removal of the diseased tonsil** before attempting the external operation upon the glands, especially in those cases in which the lymph-glands have not broken down. The extension of the infection through the lymphatics from the tonsils is thus checked.

> The writer emphasizes the importance of radiographic study in all cases of cervical, facial, and submaxillary adenitis.
>
> The external appearance of the teeth does not constitute reliable evicondition.
>
> The coöperation of the dental surgeon is indicated for the successful and expeditious treatment of submaxillary, cervical, and facial abscesses which have their origin in dental and peridental infections. B. Lipshutz (N. Y. Med. Jour., Mar. 16, 1921).

Electricity, preferably the constant current, is highly recommended by some authors. Daily sittings of ten minutes each, using 5 to 15 milliampères, are required.

Codliver oil, the iodides, and iron are indicated in all cases when the digestive organs do not rebel against their use. **Arsenic** and **strychnine** are the agents next in order, and sometimes prove very effective. **Out-of-door life** and plentiful **nourishment** are of primary importance.

> The writer emphasizes the importance of the relations between the glands in the face and neck and the teeth, tracing the development of infectious processes including adenitis, to the teeth, especially in children. **Vaccine therapy** is extolled when the adenitis is once established. If the effect of the vaccine in a few hours is slight or transient, the presence of pus is indicated and requires elimination before the vaccine can exert its efficacy. The focus must be drained continuously. He prefers for this a loop of fine copper wire, such as is used for electric light, the outer ends turned back, and the whole held in place with a strip of gauze. This loop can be inserted and removed without inconvenience through a minute incision. He prescribes flushing with an antiseptic unless the cavity be sufficient to permit the use of the Carrel method. Even when the adenitis is only indirectly connected with the mouth, the vaccine made from the mouth germs still shows efficacy. Landete (Arch. Espan. de Pediat., Aug., 1918).

CHRONIC ADENITIS.

SYMPTOMS.—The symptoms vary according to the period of development in which the diseased gland is found at the time of examination.

Three periods of development are commonly recognized in tuberculous adenitis: the period of induration, or indolence; the period of inflammation, and the period of suppuration.

1. Period of Induration, or Indolence.—This period may last for years, and resolution may even take place, though the gland always remains somewhat enlarged and indurated. The glands are felt as hard, elastic, enlarged

bodies, rolling under the finger, with more or less distinctness as they are situated superficially or deep. No heat, pain, or redness of the skin is perceived.

2. Period of Inflammation.—In this period we have pain, redness of the skin, and tenderness on pressure. The gland, if solitary, may adhere to the skin. Fluctuation may be present.

3. Period of Suppuration.—In this period we notice much more softening of the contents of the gland than a real suppuration. The skin may ulcerate through almost without inflammatory symptoms, and the contents—consisting of caseous matter half-dissolved in a whitish watery fluid—may be evacuated. When periadenitis occurs, true pus may be present.

If chains of glands are tuberculous, the latter inflame alternately and discharge their contents in the same order, a series of abscesses being thus formed.

When the contents of the gland are discharged, the skin may become ulcerated in the neighborhood, form fistulæ, and after healing leave a depressed, adherent, violet-colored cicatrix.

In some cases a fistula may form and last for years; the skin may be undermined, and disfiguring cicatrices may be formed.

Cretaceous transformation occurs at times in the deeper glands, but rarely in the superficial ones. Some caseous glands undergo a process which transforms them into a cyst-like cavity containing a serous liquid.

In chronic adenitis the glands may become painful by the compression of small nerves, or of neighboring organs; when they are inflamed a small, hard mass usually appears, either alone or united with others, which may become enlarged and suppurate, or persist with practically no change for years, or finally disappear if the cause of irritation be removed.

Chronic adenitis may assume various forms.

1. General Tuberculous Adenitis.—This presents itself especially in negroes. Organs other than the glands are but little affected, and continuous fever exists. The retroperitoneal, bronchial, and mesenteric glands are the most enlarged. It resembles in many ways an acute attack of Hodgkin's disease.

As long shown by Grancher and Marinescu, the majority of children presenting symptoms of tuberculosis also have general adenitis, the swollen glands being felt everywhere; they never change in size or consistence. Suddenly a bronchitis develops, followed by a bronchopneumonia, from which the child dies. Microscopical examination reveals caseous spots and the presence of tubercle bacilli throughout the affected glands.

Cases of cervical adenitis are usually supposed to be tuberculous, yet, according to the writer some may be gummatous, and careful study should be made to prove or disprove this supposition definitely. The clinician should obtain an exhaustive history of each case to arrive at a correct diagnosis. Coues (Boston Med. and Surg. Jour., Nov. 18, 1915).

To the familiar relation between the teeth and the cervical glands the writer also adds a mechanical factor —the pumping into adjacent tissues of *débris* through loose teeth and mastication, an open door for the entrance to the glands of tubercle bacilli. G. H. Wright (Boston Med. and Surg. Jour., Jan. 7, 1915).

In the majority of cases (80 per cent.) of chronic cervical adenitis, where no obvious source of infection is present, the tonsils are infected. The size of the tonsil makes no difference as to their infectivity, except

that the small fibrotic variety is likely to be more dangerous than the large. The organisms are present in the deepest parts of the gland. Gardiner (Lancet, Oct. 2, 1915).

The tonsils which are drained by their lymphatics into the cervical glands frequently contain tubercle bacilli. These may penetrate the tonsillar membrane without leaving any mark. In 50 per cent. of cases of tuberculous lymphadenitis, the tonsils are also infected. Hence the tonsil is an important portal for entry of the tubercle bacilli into the human organism. W. B. Metcalf (Jour. Ophthal. and Oto-Laryn., xi, 71, 1917).

[As I have emphasized in the article on the Thymus and Lymphatics (in the eighth volume) the lymphatic nodes are not mere barriers for bacteria, but protective structures in which all kinds of pathologic organisms are assailed by phagocytic lymphocytes, in order to stay as long as possible, and perhaps prevent, their penetration toward the blood-stream. While a proportion of enlarged lymphatic glands are tuberculous, others may be due to the presence in them of other organisms, a fact which imposes the necessity in all cases of ascertaining the causative agent among the many now recognized. The foregoing abstracts illustrate this fact. C. E. de M. S.]

2. Local Tuberculous Adenitis.—

(a) Cervical. This form is usually met with in children, and begins in the submaxillary glands, which are generally more enlarged on one side.

In a study of glands secured from 110 cases of cervical adenitis, and examined directly and by culture and inoculation, the writer found that of these, 10 sets of glands that were not tuberculous macroscopically, failed to produce infection in guinea-pigs. Glands from 29 other cases, all macroscopically tuberculous, and 15 of which showed bacilli on direct examination, all failed to infect guinea-pigs, the bacilli being no longer active. Glands from 71 cases produced tuberculosis in guinea-pigs. Of these, 37 contained bacilli of the human type and the 34 remaining of bovine type.

Analysis of the relative frequency of the 2 forms of infection at different age periods showed that the proportion of bovine infections was greatest in children under 5 years of age (90 per cent.), but that the bovine type of organism was by no means rare in adults over 20 years of age (23.5 per cent.). A. S. Griffith (Lancet, June 19, 1915).

(b) Bronchial. This form is thought to be always secondary to a focus in the lungs, by some authors, but this opinion is contested by many others, Osler among them. Local lung infection, pericardial infection, and general infection are to be feared, however.

(c) Peribronchial. In this form we must realize the importance of lesions resulting from caseation. There is a softening of the lymphatic glands situated around the lower end of the trachea and main bronchi. Evidence from percussion is of doubtful value; alterations in breath-sounds are much more important, especially when unilateral; divided respiration, with prolonged expiration, is found unaccompanied by any adventitious sounds. In cases in which the enlarged glands ulcerate through the air-tubes, the breath has a very offensive odor, and coexistence of fetor with hemoptysis and evidence of pulmonary consolidation is suggestive. When vomiting of blood and its passage by the bowel are added, the diagnosis of glands rupturing into the bronchus and esophagus is the most likely one.

General tuberculous adenitis is likely to occur in such cases unless prompt treatment is instituted.

(d) Mesenteric. This form may be primary, and is thus very common in

children, or secondary to local intestinal tuberculosis. The sufferers are usually weak and wasted; the abdomen is enlarged and tympanitic, and diarrhea is a common symptom. Some fever is usually present. This form may exist in adults.

Sims Woodhead found tuberculous mesenteric glands in 78.7 per cent. of necropsies on tuberculous children, and in 11 per cent. the mesenteric was the only lesion present. Colman found them in 66 per cent. of the necropsies; Walter Carr in 54 per cent.; W. P. S. Branson in 22 per cent. When this condition exists in adults, it affects oftenest the glands of the appendix or of the ileocecal region because, according to Corner:

1. The cecum is like the stomach, a resting place for the bowel content.

2. The bowel contains a maximum number of organisms in the cecum.

3. The lymphoid tissue has its greatest development in the ileum, the cecum, and especially the appendix. Louis Rassieur (Jour. Missouri State Med. Assoc., Feb., 1909).

The recognition of thoracic tuberculous adenitis in young children is at times very difficult. In 2 instances in infants studied by the writer, the symptoms from mediastinal glands included dyspnea suggesting asthma. Laryngospasm occurred. Cough was the most constant symptom—a spasmodic, dry cough, resembling that of whooping cough. Martagao (Brazil-Medico., Feb. 28, 1920).

The tracheobronchial glands are divided into 2 groups. The first or pretracheobronchial group lies in 2 parts alongside the trachea and in the superior angle formed by the trachea and the large bronchi. The second or intertracheobronchial group lies in the inferior angle formed by the bifurcation of the trachea. Clinical physical signs of enlargement of these glands are *Smith's sign* or venous hum over the manubrium of the sternum with the head in forced extension; *D'Espine's sign* of bronchophony or pectoriloquy below the level of

the seventh cervical vertebra; *Hochsinger's sign* of glandular enlargement in the fourth and fifth intercostal spaces in the median axillary line. This condition of enlargement of the bronchial glands is much more common in children than in adults, and it predisposes to the invasion of the tubercle bacillus although the primary infection may be due to grippe, whooping cough, measles, or syphilis. A radiograph will either prove or disprove its existence. Trivino (La Medicina Ibera, Mar. 20, 1920).

DIAGNOSIS.—Chronic adenitis is generally limited to one or two glands; when the glands are tuberculous, chronic adenitis is apt to affect an entire mass. The former is often associated with an external simple lesion; the tuberculous form is apt to be more frequent in children, young soldiers, and negroes.

A fragment of the suspected tissue may be implanted into the subcutaneous connective tissue of the groin of a guinea-pig, and if the specimen is tuberculous a miliary tuberculosis will develop in from five to six weeks.

The use of the tuberculin test in the diagnosis of tuberculous adenitis is reliable and harmless. The tuberculin used is a 1 per cent. solution of Koch's original product, from 1 to 5 mg. constituting a usual dose.

If in from six to twenty-four hours after the injection of tuberculin solution there occur weakness, sensations of heat and cold, general malaise, nausea, anorexia, severe headache, pain in the back and limbs, and if these symptoms are sharply defined in both their beginning and ending, reaction is considered to have occurred.

Supraclavicular adenitis, while frequent in phthisis, is not present in every case. It is, however, of great diagnostic

value when present. There may be few or many slightly enlarged glands, and they are frequently bilateral.

The writer examined over 300 children from infancy to 13 years of age from the Infants' Hospital, from a large school and from private practice, X-ray being employed to confirm d'Espine's sign. While the point on the vertebral column at which whispered voice changes from a vesicular to a bronchial character was given by d'Espine as taking place at the 7th cervical in a few cases, the writer found the change as high as the 7th cervical, but commonly at the 1st and 2d dorsal, and frequently as low as the 3d without cause. The average height was found to increase with age. [D'Espine's sign is described on page 352].

The writer, therefore, regards as a positive d'Espine a change in character of whispered voice or expiration at or below the 3d dorsal. He thinks it advisable to think of these glands as of those up and down the trachea, and of those at the root of the lungs. Inflammation of both of the sets will give positive d'Espine, dullness accompanying those at the root of the lungs, and not with glands down the trachea unless there is also consolidation at the apex of the lungs. W. W. Howell (Amer. Jour. Dis. of Children, Aug., 1915).

Lymphadenoma.—This variety of tumor is usually more voluminous and is not suppurative. The diagnosis, however, is exceedingly difficult.

Simple Adenitis.—This is an acute affection usually ending in a few days in suppuration.

Syphilitic Adenitis.—When a primary sore is present, numerous, small, hard, indolent glands can be felt if the region is supplied with a chain of lymphatics. When in secondary syphilis there is glandular enlargement, a large number of external lymphatics take part in the process.

Carcinoma.—The enlarged glands are small and hard, and can generally be distinctly traced to the growth.

Lymphosarcoma. — This persists longer and is much larger before degeneration occurs.

Chronic adenitis is frequently a complication of malignant tumors. Supraclavicular adenitis appearing during the course of visceral cancer is usually situated on the left side (found 27 times on that side by one author). It may be solitary or accompanied by adenitis in other regions; it usually appears late and develops rather rapidly. When occurring early it may be very useful for diagnostic purposes.

From a clinical point of view this adenitis may be known by its ligneous hardness, its painlessness, its freedom from adhesions, and by the union into one solid mass of all the glands forming it.

ETIOLOGY.—This form of adenitis frequently follows some neighboring superficial lesion, such as eczema, impetigo, conjunctivitis, or the exanthemata. Catarrhal inflammation of the mucous membranes predisposes to tuberculosis of the glands. The resistance of the lymph-tissue is weakened. This explains the frequent development of tuberculous bronchial adenitis after whooping-cough and measles, and of mesenteric adenitis in children with intestinal disturbances.

Cervical adenitis is not a manifestation of an already generalized tuberculosis; the bacillus penetrates, by solution of continuity of the mucous membranes or the skin, to the ganglion, which becomes a seat of infection (Duhamel).

Enlarged glands of the neck are not, primarily, tubercular, and bear the slightest relation, if any, to general or

pulmonary tuberculosis. They are due to a mixed infection of pus-producing bacilli, and will quickly resolve if the source of the infection is removed before the glandular tissue becomes disorganized.

A distinction should be made between hereditary (congenital) and acquired tuberculosis. In the latter case the author's views seem rational and correct, being comparable with and analogous to the phenomena observed in carcinoma and syphilis. When the infection is acquired there is, at first, a local seat, or focus, of infection in which the disease germs develop and from which, after proliferation, they spread until the disease becomes more or less generalized,—the germs being transmitted through the lymphatic system to the lungs and thence in the blood-stream to the various organs of the body; the various glands along the course or path of transmission become affected and in turn become additional possible foci of infection. On the other hand, when the trouble is hereditary the glandular manifestation is an indication of an already generalized tuberculosis.

Youth predisposes to caseous adenitis on account of the predominance at that period of the lymphatic system. Crowding, humidity, and bad or insufficient food are also predisposing factors. Tuberculous adenitis is frequently observed in temperate regions. Negroes brought to such climates are especially prone to become sufferers.

The absorbent power of the lymphatic system is so great that the morbific principle of tuberculosis may be transported to the glands without visible external lesion of the skin or mucous membrane.

Axillary adenitis is frequently sec-

ondary to chronic tubercular lesions of the lungs (Lépine).

The cervical glands are occasionally found affected in phthisical patients.

Observations by Mitchell, of Johns Hopkins Hospital, upon 170 cases of tuberculous cervical adenitis show the disease to be more prevalent among negroes than among whites, males preponderating over females in the proportion of 3 to 2, the majority being between 10 and 30 years of age. A family history of tuberculosis was present in about half the cases, though only 4 per cent. showed positive evidence of the disease in the lungs. The condition is regarded as a local manifestation of infection through the tonsils, adenoids, or carious teeth.

PATHOLOGY.—Usually an entire group of glands is affected. The glands are isolated when the irritation and rapidity of growth are not great; this usually occurs in secondary visceral adenitis. In other cases—especially when the glands are superficial, where the adenitis is primary—the glands are united into a large lobulated and irregular mass, the size of which may vary from that of a small nut to that of an orange.

If the adenitis follows a visceral tuberculosis the afferent lymphatics show, in some cases, signs of tuberculosis, as is the case in pulmonary and mesenteric tuberculous meningitis.

Two varieties of lesions are to be noted: 1. Lesions of chronic adenitis affecting the stroma and the elements of the gland, which becomes hypertrophied. 2. Specific lesions of tuberculosis, consisting in miliary granulation at first, ending in caseation. As one or the other of these two processes is the more prominent, so will the lesion vary in appearance. Deep adenitis is

never so sclerous as the superficial variety, the latter being characterized by a more vigorous reaction.

On section of a gland in the early stage of tuberculous infection we find it redder than usual, though at times gray and somewhat translucent. The tuberculous granules may be perceived by a glass. They are formed from the vascular and lymphatic vessels found in the cortical and medullary portions, and resemble ordinary follicles, but contain many small cells. Caseation rapidly occurs in them, beginning at the center of the cells, where giant-cells are first formed, proceeding to coagulation necrosis and caseation. A number of these granulations united form the small, yellowish masses, which may be seen by the unaided eye. Caseation is due to vascular obliteration.

The small, yellowish masses, softened at their centers, are surrounded by fibrous tissue due to sclerosis of the stroma of the gland. When this tissue gives way, several masses form a large collection of yellowish, softened material resembling putty. Calcification may occur when the process is very slow.

The specific lymphadenitis blocks the lymph-spaces and thus, for a time at least, mechanically prevents the bacilli from penetrating into the general circulation. Glands not in the stream become infected, this probably being due to the transportation by migrating cells of the motionless bacillus. However, infection usually takes place in the direction of the lymph-current. As the lymph-spaces are obstructed by inflammation products, and entrance of fresh bacilli into the gland is thus prevented, it is the multiplication of those already entered into the gland which gives rise to the tuberculosis. When caseation occurs, nearly all the bacilli have dis-

appeared, but the spores remain, and are capable of reproducing the disease. Suppuration is due to a secondary infection by pyogenic micro-organisms.

The virus of tubercular adenitis is less potent, for the caseous material of a lymph-gland kills guinea-pigs, while rabbits escape, the latter being less susceptible to tuberculous infection.

Taken as a whole, tuberculous adenitis (*a*) is a local disease which may frequently undergo (*b*) spontaneous resolution, but which (*c*) frequently tends to suppuration, the pus being nearly always sterile. It is, however, a constant danger to the system.

Chronic adenitis may, in some cases, be due to continued irritation; ulcers; chronic lesions of the skin or mucous membrane of the bones; periosteum; articulations; chronic inflammation of the viscera, and certain new growths where the adenitis is purely irritative and not yet specific.

PROGNOSIS.—A chronic adenitis may end in resolution, suppuration—caseation (see PATHOLOGY), cretaceous formation, or cyst formation. If all the tuberculous matter can be eliminated, either by nature or art, a recovery may be obtained. The deeper glands are more dangerous than the superficial, as they are extirpated with more difficulty. The great danger of local tuberculous adenitis is that it may give rise to other tuberculous lesions, either *local* (pulmonary phthisis, tuberculous osteitis, white swellings, or abscesses) or *general* (generalized tuberculosis, with rapid death).

Acute miliary tuberculosis may be caused in two ways: either by conveyance through the lymphatic system until the venous system is reached or by the perforation of a vein and the entrance of tuberculous material.

TREATMENT.—The general treatment should, in all cases of adenitis, receive considerable attention. **Good food, country air,** and **sea bathing** are of the greatest value.

In peribronchial adenitis the same general methods are to be resorted to. When due to tuberculosis and kindred diatheses and uncomplicated by fever or involvement of lung-tissue, the seashore or the country is indicated. At the seaside children should not bathe in the sea, and should be as quiet as is consistent with life in the open air. **Brisk frictions, milk, a nutritious diet,** and **iodotannic syrup** (2 to 4 teaspoonfuls per day) are effectual measures. After three to four weeks, **emulsion of calcium lactophosphate** and **codliver oil** should be given. **Counterirritation** between the shoulder-blades favors the curative action of the other remedies (Marfan). Applications of **tincture of iodine** between the shoulders, or in some cases **blisters** or, even better, **ignipuncture,** will fulfill the latter indications. The syrup of the **iodide of iron, tincture of iodine, potassium iodide,** or large doses of **codliver oil,** already mentioned, either alone or with **cinchona wine, arsenic,** or **arseniate of sodium,** are the standard remedies usually recommended in these conditions. Not much is to be expected from them, however, unless **outdoor life** is insisted upon.

Extirpation is indicated when internal remedies and **X-rays** have failed; when glands involve the face and produce deformity; when they are isolated and few in numbers; when they have undergone fibrous degeneration; when they are not freely suppurating. It is contraindicated when there is impaired general health and tubercular deposits in the lungs and joints; when ramifications of the chain of glands are very extensive.

The writer treated 30 cases of tuberculous adenitis with **X-rays,** and obtained prompt recovery. It proved so effectual that it can be relied on to differentiate ordinary tuberculous glands from Hodgkin's disease, as in his 5 cases of the latter disease not the slightest benefit was apparent. It even seemed, in fact, as if some of the cases had been aggravated. J. and S. Ratera (Siglo Medico, July 21, 1917).

In a group of 48 cases of tuberculous glands, complete cure was realized in 35. Only 2 others failed to show marked benefit, though improved. A great advantage of the treatment is that the healing proceeds without leaving disfiguring traces. From 8 to 10 exposures were the average course, some cases needing very few and others requiring a whole year. The exposures were about 4 H. units and the intervals about 3 weeks. Van Ree (Nederl. Tijdsch. v. Geneesk., Sept. 1, 1917).

Cervical adenitis is a frequent disease and deserves more serious consideration. Each case should be studied as an individual, and every means employed that will produce beneficial results. **Röntgen rays** can be expected to relieve completely the early cases. Softened glands should be **opened** and **drained** as abscesses. Patients who have been operated upon should receive postoperative treatment to prevent recurrences. G. E. Pfahler (N. Y. State Jour. Med., xviii, 99, 1918).

The end-results in the treatment of tuberculous adenitis by **X-rays** are superior to those produced by any other method, because radiation is a local as well as a constitutional treatment. More cases are permanently cured by this method than by surgery alone. Röntgenotherapy never spreads the tuberculous process, leaves no deformity, and the patient always gains in weight and general health during treatment. R. H.

Boggs (Amer. Jour. Roentgenol., v. 425, 1918).

Brilliant results reported from **radiotherapy** of tuberculous glands. Improvement obtained in all of 470 cases and a clinical cure in 85 per cent. within a few months. The more malignant processes usually require preliminary surgical measures. The benign type may be larger, but they retrogress under a few exposures. A cheesy agglomeration of lymphomas may require 6 or 8 exposures at 3-week intervals, and after this a few treatments at 3-month intervals. The cheesy matter can be aspirated through a large needle, and any particularly favorably located single gland can be excised. Painful glandular processes, if solitary, had better be excised, followed by 6 exposures. If inoperable, the exposures alone must be the reliance. When combined with an abscess, the writer advises incision with 1 exposure a week, never exposing red skin; otherwise scarring results. Van Ree (Nederl. Tijdsch. v. Geneesk., Nov. 13, 1920).

The possibility of giving rise to a tuberculous process elsewhere by facilitating absorption through exposed tissues should be borne in mind.

In all cases of cervical adenitis the **tonsils** should be **removed** as the first procedure. If the glands are not broken down, and an operation on them has to be performed, then the tonsil should be removed at the same time. Removal seems to be followed by no deleterious effects, while the tonsil may afford entrance for rheumatic infection. Richards (Boston Med. and Surg. Jour., Jan. 7, 1915).

As shown below prudence is necessary in the removal of diseased tonsils, lest general infection result if tubercle bacilli are present. Pottenger deems it necessary to emphasize the importance of prudence in this connection. Our own practice is to give the **iodides** internally and to treat the tonsils by means of the **curette**, the **phenolated iodo-tannin glycerite** (see vol. vii, page 73) and **galvano-cautery** if necessary to close the crypts, removing the tonsils

only if necessary after these procedures have greatly reduced or eliminated the danger of systemic infection. EDITORS.

Senn held that early **operative interference** is, as necessary in the treatment of tubercular adenitis as in the treatment of malignant tumors, and holds out more encouragement, so far as a permanent cure is concerned. Tillmann argues that glandular tuberculosis should be operated as soon as possible, in order to prevent general miliary tuberculosis by the passage of the bacilli into the system.

The treatment by **filiform drainage** is simple and easily carried out under local or no anesthesia, and results in a cure, without any noticeable scarring, in about 2 weeks. In *small, superficial, closed, cold abscesses* in which the overlying skin is not inflamed, he passes a large needle completely through the lesion, carries 2 strands of horsehair through it, knots them to form a loop, passes through 2 more strands perpendicular to the first 2 (crucial drainage), and applies a dry **zinc peroxide dressing.** In large, deep abscesses of the same kind he makes a narrow, stab incision, explores the abscess cavity and its pockets, with a probe or fine grooved director, and passes horsehair from the central incision through the two poles and the various pockets of the abscess (radial drainage). Where the skin is inflamed it can be kept from ulcerating by inserting crucial horsehair strands through the abscess from the sound skin; if perforation of the skin does take place it soon closes under a dry zinc peroxide dressing. Chaput (Paris méd., Apr. 22, 1916).

Rapid and complete healing is always realized in the writer's cases after **excision of tuberculous glands** in the neck, owing to his routine procedure of suturing immediately without draining. In more than half of his 63 cases the gland burst and pus inundated the field, but his assumption that the pus in such cases is

sterile was always confirmed by the healing by primary intention. Dufourmentel (Presse méd., Dec. 5, 1918).

After **incision, closure** should be performed. The wound should be **drained.** The operator should not only feel, but see, every gland he removes. In cervical adenitis an S-shaped incision gives more room and a better cicatrix.

In other regions the incision should be made so as to bring its axis parallel

Sigmoid incision for the removal of cervical glands.   (*Senn.*)

with the cutaneous folds. Local recurrence should be treated in the same way. Three or four operations in as many years have been performed by Senn on the same patient, with final successful result.

Mitchell, of Johns Hopkins Hospital, uses a T-shaped incision when making a radical operation for removing all the glands and surrounding fat. The long arm of this incision is made to curve forward over the sternomastoid muscle and starting from the mastoid process joins the short arm along the clavicle, the dissection being carried from below upward and outward from the mesial line, the external jugular vein being tied with two ligatures and divided between them. The omohyoid muscle is then divided, and by using it as a retractor the internal jugular vein is exposed and the sternomastoid muscles pulled aside. In dissecting out the mass of glands the greatest difficulty is experienced with the chain connecting the anterior and posterior triangles behind the sternomastoid muscle, as the spinal accessory nerve passes through the mass and is generally very adherent. It is only when there is very extensive mischief that it becomes necessary to divide the sternomastoid muscle or spinal accessory nerve, or even to tie and divide the internal jugular vein, and these steps should only be resorted to when the advantages of free exposure outweigh other considerations. The wound is closed with a subcutaneous silver suture and drained at its most dependent part. The resulting scar is usually slight.

When many glands are involved and suppuration has occurred, or when periadenitis is present, excision is not to be recommended, as extensive connective-tissue infiltration renders it impossible to remove all the infected tissue.

Subcutaneous extirpation may be resorted to, but the method allows of but imperfect evacuation of the glandular contents and is unsatisfactory.

Drainage of the abscess is a measure which may be recommended for many reasons. A small incision is sufficient for all purposes, and there is practically no scar left.

Mesenteric tuberculous glands should be removed if possible. They are usually discernible as persistent movable tumors beneath the abdominal wall, with anorexia, loss of weight and strength, occasional fever, colicky pains, and possibly mucous in the stools with a tendency to diarrhea.

Less radical measures sometimes bring about a cure. A transformation of the tuberculous tissues into a sclerotic mass may be obtained. A solution of **chloride of zinc** injected about the tuberculous foci excites a growth of new fibrous tissue, which encapsulates the diseased portion.

Solutions of **iodoform** and **ether** (iodoform, 1 part; ether, 5 parts; distilled water, 5 parts. Injection not to be repeated while iodoform is being excreted in the urine), after Verneuil, in cases where operative procedures are indicated, give a lasting cure, without a cicatrix. These injections seem to exert a beneficial action not only on the tuberculous glands treated, but also on those at a distance from the seat of the injection. Robin uses an injection, **iodoform, 1** part; **ether, 10** parts; **oil of sweet almonds, 100** parts; **creosote, 2** parts.

Camphor-naphthol has proved valuable in some cases. It is prepared as follows :—

R Betanaphthol,
    Camphor ....āā 10 parts.
    Alcohol (60 per cent.) ...... 40 parts.

A few drops are to be injected, with antiseptic precautions, here and there throughout the mass of indurated glands, as suggested by Courtin, of Bordeaux.

It is claimed in favor of camphor-naphthol that there is no danger of intoxication and that the treatment is almost painless. Ménard and Calot, however, have reported cases of intoxication following injection of camphor-naphthol into abscess cavities. The patient suffered from frequent, rapid pulse, loss of consciousness, and epileptiform attacks. The quantity of the drug injected was about 6 drams. This patient recovered. In another case, 8 years of age, 1½ ounces of the solution were injected. In the third case, aged 12, 5 drams. In the last 2 cases life was saved by freely opening the cavity and washing it out on the first appearance of toxic symptoms.

Interstitial injections, of **iodine**, frequently recommended, usually fail or cause suppuration, owing to the fact that the tincture of iodine is employed. **Metallic iodine,** however, gives good results; the abscess is filled with the crystalline iodine, 8 or 10 applications usually insuring a cure.

Exposure to **sunlight** constitutes the most eligible conservative treatment, being preferable because it acts upon the entire body while taking the patient away from his ordinary mode of life. Iselin (Correspondenzbl. f. schweizer Aerzte; Wiener klin. Woch., Nu. 45, 1912).

Barjou, of Lyons, commends the use of the **X-ray** in the treatment of tubercular adenitis. The principal effect of this treatment is upon the general infiltration which so often accompanies scrofula, uniting the lymph-glands in a solid mass. The glands become separated soon after beginning the applications, and later disappear. If there is any tendency to softening, the rays hasten this, so that the abscess may be opened earlier. The rays continue to have a good effect upon the suppurating tissues. Untoward effects or tendency to cause metastasis are rarely noted. The late C. L. Leonard deemed it the most effective method for the treatment of tuberculous adenitis in all its varieties. It affords also the best cosmetic, as well as permanent, results. Much evidence to this effect was adduced in the foregoing pages.

Cases of tuberculous adenitis were formerly given X-ray treatment to avoid unsightly scars, but to-day it is

used because operation is followed by frequent recurrence. The **X-ray** treatment is preferable when the glands are scattered or broken down. Boggs (N. Y. Med. Jour., May 27, 1916).

Twenty cases of tuberculous adenitis treated successfully with **radium**. The nodes at all stages disappeared, leaving no scar unless a sinus had been present at the beginning of the treatment. Ulceration did not occur in any case. Fifteen milligrams of **radium bromide** spread over an applicator 1¼ inches in diameter, screened by 1 millimeter of silver, was strapped over the area to be treated for 10 hours. Two applications a week were usually employed. After a week or 10 days the swelling began to grow smaller and at the end of a few weeks nothing but fibrous nodules were left. E. S. Molyneux Brit. Med. Jour., Nov. 29, 1919).

Koch's tuberculin and the simultaneous use of the **Bier method** have been used with success in tuberculous adenitis.

At the Westfield State Sanatorium, Mass., patients having no more than 1 degree of temperature, and having no other signs of active pulmonary disease, are given **tuberculin** treatment, the bacillin-emulsion being used. The initial dose is one-millionth of a milligram and the course of treatment extends over a period of about 6 months until the maximum of 10 milligrams is reached. The glands decrease perceptibly in size and the area of dullness over the hilus becomes less pronounced. **Surgical interference** is necessary to remove only such glands as have become caseous or fibroid. H. D. Chadwick (Boston Med. and Surg. Jour., Jan. 7, 1915).

Of 40 cases of surgical tuberculosis treated by the writer with **tuberculin**, 19 had glandular disease of the cervical group, 1 case showing also involvement of the axillary group. Of the joint cases, the hip was involved in 6. In 4 cases the vertebræ were affected. Of the 19 cases, 12 were discharged as well, 6 improved, and 1 unimproved when last seen. Sieber (Amer. Jour. Med. Sci., Sept., 1917).

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ADENOID VEGETATIONS.—

DEFINITION.—A definition of *adenoid vegetations,* or *adenoids, must be* somewhat elastic. The name *tonsil* is often applied, and we hear pharyngeal tonsil, third tonsil, Luschka's tonsil, or bursa, used indiscriminately. It would be well to restrict the term *tonsil* to the lymphoid aggregation between the pillars of the fauces, where it was first employed. The word *adenoid* seems to have been proposed nearly two thousand years ago (Wright, "The Nose and Throat in the History of Medicine"), is therefore sanctified by time and usage, and will doubtless be permanently retained.

Lymphoid tissue is a normal constituent of mucous membranes, but the question: When does it become pathological? is not easy to answer. On the one hand we are told that it is abnormal "when visible to the naked eye," and on the other "when it causes subjective symptoms." Many insignificant hyperplasiæ cause a good deal of disturbance, and on the contrary in a stolid, phlegmatic child or in a pharynx of large dimensions very considerable hypertrophies often seem to interfere but little with comfort or health. An accurate definition is desirable, but in view of the fact that lymphoid tissue is a recognized avenue for invasion of the system by pathogenic germs it is most important to determine in what condition of this tissue, healthy or diseased, the process of invasion is favored. Clinically it is clear that, when diseased, it is no longer capable

of performing its physiological function and is a detriment to health quite apart from effects due merely to mechanical obstruction. The general symptoms present can hardly be explained on the latter ground alone. A species of toxemia must be also concerned. Distended crypts provide an excellent bed for the cultivation of germs, which find ready access to the circulation in the absence of effective resistance. Lymphoid tissue may be a portal of entry without itself showing marked pathological change, while it is probable that a dense fibrous adenoid, as met with in older subjects, may offer a firm barrier to bacterial assaults.

In keeping with Harris and others, the writer looks upon adenoids as defensive structures in prolonged exposure to pathogenic agents. S. G. Vicente (Rev. de Med. y. Cir. Pract., July 14, 1915).

The writer lays stress on the close relationship between the nasopharyngeal glandular structures (adenoids, etc.) and the pituitary body. Not only are the functions of the latter morbidly influenced, but the results of adenotomy or other local treatment of these pharyngeal tissues— rapid growth and improved nutrition, relief of aprosexia and morbid somnolence, etc.—indicate to what extent the pharyngeal tonsil and the pituitary system are related. The cases of retarded growth relieved by adenotomy suggest, moreover, that adenoids inhibit the nutritional or developmental function of the pituitary system which we have come to understand as necessary for normal development. In a former article the author pointed out that the "adenoid" region was the part of the nasopharynx most assailable by infection, and that the angle of this region was the most vulnerable spot in the whole body. W. Sohier Bryant (Amer. Jour. Med. Sci., July, 1914; Med. Rec., Sept. 9, 1916).

In certain adenoid subjects a psychic syndrome may be observed, especially in adolescence, which consists in a marked deficiency in memory, somnolence or insomnia, lack of power to fix the attention, and in intellectual weakness. This syndrome may even be observed in various diseased conditions of the nasopharynx and sphenoid regions, especially tumors. It is probably of hypophyseal origin. The writers report the details of 3 cases observed in soldier, having a history of adenoids which had not been treated and remnants of which still persisted. The syndrome was marked in all 3, along with very manifest feminism. Citelli and Caliceti (Policlinico, xxv, sez. prat., 245, 1918).

SYMPTOMS AND DIAGNOSIS.

—It is not safe to rely upon the so-called "adenoid facies" as a diagnostic sign. A very similar appearance is sometimes seen in a subject of intranasal obstruction, while the postnasal space is quite free. A typical case of adenoid hypertrophy in the vault of the pharynx usually wears a dull, listless expression. The nostrils are narrow and pinched; the bridge of the nose by contrast seems widened. The upper lip is retracted, exposing the teeth of the upper jaw, which project and overlap those of the lower. The upper jaw is compressed laterally, so that the roof of the mouth is converted into a Gothic or V-shaped arch. Deflection of the nasal septum may be a result. The nasolabial folds are effaced, and the transverse vein at the root of the nose is unusually conspicuous (Scanes Spicer). The child has a pasty, sallow complexion, and the cervical glands are prominent. The nutrition of a nursing infant suffers in consequence of frequent interruptions due to need of getting air through the mouth. For a similar reason older children "bolt"

their food, which being defectively insalivated causes gastric derangement. The latter is further aggravated by catarrhal secretion, always in excess in these cases, finding its way into the stomach. Loss of appetite and malassimilation are natural sequels. In severe cases deformity of the chest, pigeon-breast (Dupuytren), results from the bad constitutional state, the labored breathing, or from both combined. The mental dullness shown by these children is referred to interference with the lymphatic drainage of the brain and to impaired hearing.

An investigation of the occurrence of adenoids in three London elementary schools, with an attendance of 2315, showed that, on the average, about 37 per cent. of the children in elementary schools have adenoids, and that between 72 and 76 per cent. of these have enlarged tonsils as well. On the average, 31.2 per cent. of adenoid cases are mouth-breathers, complete or partial, and hypertrophy of the faucial tonsils may give rise to mouth-breathing in the absence of adenoids. Sex appears to have no influence upon the incidence of adenoids. Adenoids are more common about the age of 8 years, and are next most frequent at about 12 years. True aprosexia is often confused with apparent dullness, due to defective hearing, and it occurs in only about 4.7 per cent. of adenoid cases, is more frequent in girls, and, when present, is associated with a marked degree of adenoids. Macleod Yearsley (Brit. Jour. Child. Dis., Feb., Mar., 1910).

Gritting of the teeth at night was noted in 34.4 per cent. of a series of 500 cases of adenoids by the writer, and is believed by him of diagnostic value. Benjamins (Nederlandsch. Tijdschr. v. Geneesk, July 17, 1915).

"Growing pains" are due to adenoids in fidgety children with constant slight fever, slight cervical glandular enlargements, and a muffled first heart sound; great improvement follows adenoidectomy in these cases. H. O. Butler (Lancet, June 26, 1915).

The term *aprosexia* has been given to lack of ability to concentrate (Guye). Mouth-breathing is a source of much discomfort and even danger. The membranes of the whole respiratory tract suffer from inhalation of improperly prepared air.

Snuffling and noisy breathing by day and snoring at night are often distressing. Sleep is much disturbed thereby as well as by bad dreams, "night terrors" (*pavor nocturnus*) resulting from deranged cerebral circulation. The effect upon the voice is characteristic. Its non-resonant, "dead" quality always suggests adenoids, at least in young subjects. The ability to precisely locate an obstruction from the sound of the voice, claimed by some, seems to be hardly warranted. In addition to special difficulty with the nasal consonants speech in general is thick and unpleasing. Actual stammering and stuttering have been ascribed to adenoids, and a long list of reflex neuroses affecting the eyes, the ears, and more remote organs has been compiled. Among them may be mentioned laryngeal spasm, hiccough, asthma, hernia, prolapse of the rectum, nocturnal enuresis, chorea, and epilepsy, some of which no doubt have their origin in the imagination of the observer. The relation of laryngeal neoplasms to adenoids is a question of much interest. Even if we decline to accept a theory of "verrucous diathesis," or special predisposition to neoplastic development, it is reasonable to assume that habitual mouth-breathing must irritate the laryngeal mucosa. It has also been suggested that secretions find their way from above into the vestibule of the

larynx, and, again, that the extraordinary labor imposed upon the larynx during phonation under these circumstances favors the formation of new growths.

Many excellent observers maintain, however, that neoplasms of the larynx are not especially common in adenoid cases. Frequent attacks of earache,

In a large number of school children who suffered with blurring vision and fatigue on reading, the author found nasopharyngeal hypertrophy to be the real cause of the symptoms. W. M. Killen (Brit. Med. Jour., Sept. 25, 1909).

The writer observed a child with mild bilateral exophthalmos, relieved by adenoidectomy. W. C. Posey (Pa. Med. Jour., July, 1912).
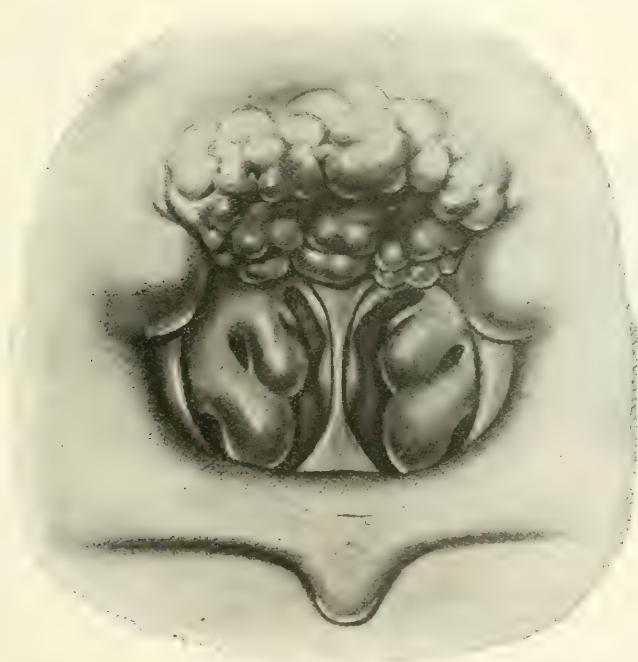
Posterior rhinoscopic view. (After *Grünwald.*)

of nosebleed, and a tendency to catch cold, are generally included in the list of symptoms. Headache and asthenopia are complained of, the senses of smell and of taste are impaired, and frequently an ichorous discharge excoriates the nostrils and upper lip. Attacks of petit mal in a child may also be due to adenoids.

Impairment of hearing, chronic otorrhea, profuse nasal discharge suggesting sinusitis and sinusitis are frequently associated conditions.

The picture in the rhinoscopic mirror is unmistakable. Lobulated or fissured masses of various sizes are seen hanging from the vault of the pharynx, obscuring the arches of the choanæ, and often filling the fossæ of Rosenmüller and covering the orifices of the Eustachian tubes. They have been likened in appearance to a "cock's comb" (Czermak, 1860), and they are spoken of by Voltolini (1865) as "stalactite-like growths," a term adopted by Morell Mackenzie. They are often

visible by anterior rhinoscopy when the intranasal structures have been shrunken by atrophy or retracted by cocaine. Sometimes the vegetations are distributed down the posterior wall of the pharynx, below the plane of the velum, or they may push forward into the nasal chambers. The view may be masked by viscid or in-spissated secretion, and, being fore-shortened in the mirror, does not give an adequate idea of the volume of the growth. In some cases, generally in

Adenoids seen through anterior nares.
(After *Grünwald*.)

older subjects, the mass is more uni-form and cushion-like in appearance, or is bilobed, being divided by an anteroposterior median furrow (*reces-sus pharyngeus medius*), and is less vascular looking. In adults remnants of adenoids are often seen in the form of bands between the Eustachian cushion and the pharyngeal wall, which doubtless bear some relation to various subjective aural disturbances.

Applications of cocaine and the use of a palate retractor are to be recom-mended only in older children and when a rhinoscopic examination is imperative. By the exercise of tact and patience it is often possible to get a view, even in a very unpromising case.

In some it is out of the question and the only resource is a digital examina-tion. The process is disagreeable to the patient and dangerous for the examiner in children, unless one's finger is pro-tected in some way. A finger shield of metal or rubber may be used, or a mouth-gag may be applied. Better still, the child being firmly held by an assistant, the examiner standing on the left presses the right cheek of the patient between the separated jaws with his right middle finger while he quickly passes his left forefinger into the open mouth and up behind the velum. The mouth cannot be closed and thus the finger is safe.

The anatomical landmarks to be sought are the posterior margin of the vomer in the middle line and the Eu-stachian eminences at the sides. A novice might mistake a prominent Eustachian cushion, a papillated pos-terior end of an inferior turbinate, or even the contracted velum (F. H. Hooper) for an adenoid mass, but the last is higher in the fornix of the pharynx and more posterior and has a distinctly lobulated, elastic, and pulpy feeling, compared to that of a bunch of earthworms. On withdrawal the fin-ger is smeared with blood, which is not the case when a healthy pharynx is ex-plored, unless excessive force has been exercised. In those who object to the finger some idea of the extent and con-sistence of a postnasal growth may be gained by palpation with a stiff probe or the edge of a rhinoscopic mirror. In some cases a very beautiful view of the vault of the pharynx is given by the ingenious electric pharyngoscope de-vised by Hays. The end of the instru-ment having been passed into the oro-pharynx the patient is instructed to close the lips and breathe quietly

through the nose. The palatal muscles relax and permit the light to flood the cavity of the rhinopharynx. With a little patience and care a complete picture may be obtained, even in very sensitive throats. Nasal polypi, retropharyngeal abscesses, syphiloma, and neoplasms, benign or malignant, may occur in this region, but usually present features or give a history which serve to distinguish them.

> Benign nasopharyngeal polypi, studied in 22 cases. They are usually unilateral and solitary, and have a peculiar pear-shaped form, the broad end lying in the nasopharynx, while the stalk extends into the nose. They may attain considerable size, and are subject to inflammatory changes which may end in partial or total gangrene. The treatment is very favorable, as they are easily laid hold of, and readily torn out on account of their slender stalk. In the majority of cases the polypi do not recur.
> There is usually a profuse discharge of serous fluid after the extraction, and examination of the antrum shows a slight chronic inflammation. Choanal polypi originate within the antrum of Highmore, and are due to inflammation of the antral mucous membrane. Killian (Lancet, July 14, p. 81, 1906).

It is hard to believe that a simple pendulous polypus of the nasopharynx could be mistaken for a bunch of adenoids. Yet the risk is evidently present in the minds of some observers. In a paper by W. A. Wells (Laryngoscope, July, 1911) the fact is noted that it is usually taken for granted that postnasal obstruction in a child under 15 years is due to adenoids. He describes 3 cases of fibrous polypus, which he makes the basis of a plea for intranasal removal with the cold-wire snare rather than by a "mutilating" external operation generally employed in growths of this kind. He enumer-

ates three theories of etiology: (1) cranial, propounded by Nélaton; (2) choanal, that is, springing from the ethmoid, sphenoid, or vomeral region, and (3) sinusal, as adopted by Killian in the paper above quoted. While it is well to bear them in mind, fibrous polypi of the pharynx are so rare and their symptoms are so different from those of adenoids, except in the single feature of obstruction, that the chance of confusion is rather remote.

Rugæ or folds of thickened mucous membrane in the floor of the nose, and the so-called "lateral bands" of red and thickened membrane on the walls of the pharynx behind the posterior pillars (*pharyngitis lateralis hypertropica*) are regarded by some as pathognomonic, but each is often found without adenoids. Fluid injected into one nostril is expected to escape by the other if the nasopharynx is free; by the mouth if adenoids are present (Semon, quoted by Schech). A similar test with oil spray is regarded as "almost absolutely diagnostic" (Bosworth). Each of these experiments must be invalidated by a unilateral nasal stenosis and should not be relied upon.

Adenoids may exist without enlarged faucial tonsils: the reverse is seldom true. Hence it is important to examine the pharyngeal vault in all who manifest the latter condition. The occurrence of adenoids, as well as of turbinate hypertrophy, in victims of cleft palate has often been remarked, whether as an effort of nature to stop the gap or as a consequence of the same diathesis that caused the palatal deformity is hard to decide. Such cases afford unusual opportunity for study of these anomalies.

ETIOLOGY.—A constitutional state allied to struma, termed *lymphatism*

(Potain), predisposes to lymphoid hyperplasia. From observation of 1995 cases Sendziak concludes that "scrofula" plays an important part in etiology, a view shared by Lennox Browne. The exanthemata, syphilis, tuberculosis, are similarly accused. Poor sanitation, bad hygiene, and improper diet are undoubted factors, yet not infrequently cases occur in which none of the foregoing elements is concerned and we are at a loss to discover the cause of the condition.

The importance of nasal stenosis, resulting perhaps from some injury in early life, is generally admitted. Behind an obstruction the air is so rarefied on inspiration that congestion of the mucous membrane results with consequent tendency to hyperplasia. The bearing of this fact with reference to treatment should be appreciated. The habitual breathing of impure air, or of air too hot or dry, often prevailing in our homes and sleeping rooms, no doubt has a bad effect on the mucous membranes. The same is true of certain occupations that involve the inhalation of irritating vapors or floating matter in the air. The condition occurs with equal frequency in the two sexes. It seems reasonable to admit an inherited proclivity. Those who deny the existence of heredity find it difficult to explain the exhibition of almost identical local conditions in several successive generations. The effect of a rigorous climate is not necessarily bad, but extremes and sudden changes of temperature and humidity are no doubt harmful.

Adenoid growths are essentially a disease of early life, of the formative period, when the lymphoid tissues are especially active. A few congenital cases are on record. Among 437 children in the first three years of life examined by W. F. Chappell not a single example of lymphoid hypertrophy under the age of three months was found.

R. G. Freeman has rightly criticized the neglect of adenoids in early infancy, as they interfere with the proper development of the child by reflex action, by the irritation they produce and the obstruction they cause. The postnasal pharynx at birth is a space only one-quarter inch high by one-third inch wide, so that a very slight adenoid hypertrophy at this period will cause obstruction. At the end of the first year it is nearly doubled in size. It often produces symptoms in the first days of life, and the mistake is sometimes made of diagnosing specific disease. The snuffles are specially marked while the child is nursing and result from an adenoid which produces irritation, and, if large enough to obstruct the pharynx, there is mouth-breathing.

A survey of 1064 operations for the complete removal of tonsils and adenoids caused the writer to wonder whether all these operations are really necessary. The removal of adenoids in the so-called idiopathic asthma of the nervous, wheezy child has no beneficial effect, and most of these children have no adenoid growth. Idiopathic asthma must not be confused with the intermittent suffocative attacks during sleep, which are due to adenoids, and are cured by the removal of the growth. A large number of children have attacks of earache and deafness during colds, with retraction of the drums, which frequently suppurate; and if such a case is allowed to continue without operation, the deafness or dullness of hearing becomes permanent, and is beyond cure. The affection of the ears makes operation imperative. The writer has carefully examined a large number of children 6 months or more after operation, and has endeavored to follow up cases, and has not observed any deleterious effects

or disadvantages following removal of tonsils and adenoids. He has not obtained any evidence to indicate that the removal of the tonsils predisposes these children to diphtheria, scarlet fever, or other acute infections, but has seen several cases of unhealthy spongy tonsils yielding cultures of the Klebs-Loeffler bacillus weeks after the quarantine period had elapsed. E. D. D. Davis (Brit. Med. Jour., Jan. 26, 1918).

Numerous statistics are available showing a preponderance of evidence that removal of diseased adenoids and tonsils decidedly lessens the susceptibility to the contraction of the acute exanthematous diseases.

Rare instances have been noted in the aged, but the tendency is toward atrophy after puberty. Several cases in elderly people have been observed by Bryson Delavan, who holds the belief that the condition may develop in middle life and is not necessarily a legacy from childhood. One was discovered by J. Solis-Cohen in a woman of 70, and a number of authentic cases after the age of 60 have been reported (P. G. Frank), but at this time of life a malignant element is always to be suspected. The curious observation has been made by Gellé that these structures sometimes show renewed activity at the menopause.

The bacteriology of adenoid tissue is very similar to that of the tonsils, among the infective organisms being staphylococci, pneumococci, streptococci and at times the Klebs-Loeffler bacilli and the tubercle bacilli. A surprising number of cases show the streptococcus hemolyticus and streptococcus viridans.

PATHOLOGY.—Lymphoid cells embedded in a reticulum of connective tissue containing small blood-vessels and nerves, the retiform adenoid tissue of His, and enclosed in a mucous membrane covered by columnar ciliated epithelium, constitute adenoid vegetations. The relative proportion of these elements varies with the age of the patient, the duration of the disease, and the frequency and intensity of acute inflammatory attacks, to which this tissue is very liable. In young subjects cells predominate and the tissue is soft, friable, and vascular; in older ones connective tissue is in excess and the mass is more dense and hard.

As a matter of clinical convenience adenoids are sometimes divided into soft and hard, which are, of course, merely grades of the same pathological process. In very young children, also, a temporary intumescence takes place in consequence of gastrointestinal disturbance or other cause, when many of the subjective symptoms of adenoids are presented. This condition, naturally, calls for different treatment than an organized hyperplasia. Morbid changes are not confined to the epipharynx, but involve adjacent lymphoid structures. Cystic transformation and other disorders of the pharyngeal bursa have been particularly described by Tornwaldt. A cyst of the bursa may reach extreme dimensions and occasionally small cysts are met with in the adenoid tissue, but the importance of these conditions has been somewhat exaggerated. The idea once expressed by Woakes that adenoid vegetations are papillomatous is not sustained.

PROGNOSIS.—Under present-day methods of attacking the disease the prognosis is good, both as to arrest of the morbid process and relief of associated symptoms. Only in case the condition has been extreme in degree or

duration organic changes may have been established, for example in the ears, which are irremediable. Chronic otorrhea due to adenoids cannot be cured while the latter are allowed to persist. Likewise impaired hearing and tinnitus due to occlusion of the Eustachian tube from pressure or congestion must be reached through removal of an adenoid mass. Recurrence of adenoids may take place in certain cases of pronounced lymphatism (status lymphaticus), in which predisposing factors cannot be wholly eliminated, or when an operation for removal has been done very early in life. The suspicion remains, however, that some alleged relapses are really examples of incomplete removal. These partial operations are explained in a measure by A. A. Bliss on the ground that the lymphoid tissue penetrates the fissures of the vomerosphenoidal articulation (*canales basis vomeri* of Harrison Allen), where it is more or less inaccessible. Extreme vascularity of the region and the fact that the adenoid is often made up of separate and distinct bundles also contribute to the possibility of apparent recurrence, which is really a growth of tissue that has evaded the knife.

It is safe to say that no operation in the upper air tract confers more gratifying and positive benefits than an adenectomy properly done. There has been much controversy as to the thoroughness with which morbid tissue should be removed, one side advocating extirpation of every vestige and the other averring that such a course is ultraradical. When we reflect upon the wide distribution of lymphoid tissue in the so-called ring of Waldeyer, or lymphoid triangle, the conclusion is forced upon us that absolute eradication is impracticable, even if desired.

What we accomplish in a given case is extraction of the most salient and diseased portions: the consequent improvement in air supply and in other respects enables nature to do the rest. This statement is not to be taken as a defense of superficial operating, or as a suggestion that we may trust nature to supply defects involved in our own negligence. Postoperative shrinkage of any considerable remnants is not to be expected, these fragments showing rather some apparently compensatory hypertrophy, yet there are limits of safety beyond which we may not pass and anatomical conditions which are insuperable. Certainly erosion of the mucous membrane through its whole thickness, so as to replace glandular tissue by scar tissue, is inadvisable.

Adenoid tissue is present in the vault of the pharynx in 1 out of every 4 recruits. It should be recorded in the physical examination so that due weight may be given to it as a factor in producing defective hearing when cases of this sort come up for discharge for disability or pension. All large adenoids should be excised on entry into the service, and smaller masses if associated with pathological changes in the middle ears. Refusal to consent to operation should disqualify applicants for enlistment in the artillery branch of the service or transfer to that branch. Every 2 out of 3 recruits who have adenoids have visible changes in the middle ears. Fifty per cent. of the cases who do not have adenoids, but who do have hypertrophied tonsils, have changes in the middle ears. Changes in the middle ears without the presence of either adenoid or tonsillar hypertrophy are unusual, and occur in only 1 case out of 12, and in the case in which it occurs it is usually associated with hypertrophic rhinitis. In other words, in 11 cases out of 12 which show changes in the middle ears, adenoid or ton-

sillar hypertrophy will be found. One out of every 3 cases with adenoids will also have hypertrophied tonsils. Two out of every 3 cases with hypertrophied tonsils will also have adenoids. Recruits with marked hypertrophy of the tonsils should have the glands excised, whether they have had repeated attacks of acute tonsillitis or not. Adenoids do not undergo spontaneous atrophy in young adults. Le Wald (Military Surgeon, May, 1910).

In a small proportion of cases breathing by the natural channels is not at once resumed. This is due simply to the *habit* of mouth-breathing, or to imperfect development of the air tract from prolonged disuse. In the former case the habit is soon corrected by some device for binding up the chin and keeping the mouth closed during sleep. In the latter the difficulty is greater and it may be a long time before the normal respiratory current is restored. These cases, fortunately rare, are most disappointing to operator and parents and yield, if at all, only to careful attention to hygiene and to measures tending to promote development. The co-operation of the dentist is enlisted for correction of the oral deformity, widening the dental arch and thus depressing the floor of the nose and increasing the diameters of the nasal passages. It is best not to delay this beyond the sixth or seventh year (E. A. Bogue), although surprising results may be achieved much later.

In some cases mouth breathing develops without any malocclusion or nasal obstruction, the mouth simply being involuntarily relaxed. This is corrected by forced nasal breathing at night through the use of lip and chin bandages. Skilful massage of the relaxed tissues is also helpful. O. W. White (Jour. Amer. Med. Assoc., Sept. 25, 1915).

Two other causes of continued difficulty in breathing after adenectomy have been described: one is extraordinary prominence of the bodies of the cervical vertebræ (J. E. Newcomb), and the other is a paresis of the suspensory apparatus of the hyoid bone and the tongue, so that, when the muscles are relaxed in sleep, the tongue falls back and occludes the glottis (Harrison Allen).

In the experience of Payson Clark mouth-breathing persisted in 35 out of 75 cases whose subsequent history could be learned. Over 500 others were not traced and it is fair to assume that the above percentage might be greatly reduced.

Faulty habits of speech are to be reformed by careful exercises under competent supervision. The palatal muscles having been long curbed in their action need to be properly educated.

TREATMENT. — Until Wilhelm Meyer, in 1868, gave to the world the results of his careful studies, but little had been done in diagnosis or treatment of adenoids. A few scattered references are found in literature many years before his day, and the valuable researches of Luschka and others in the anatomy of this region are well known, but no serious attempts were made to remove from the postnasal region certain obstructions, and their exact nature was not fully understood until Meyer began his investigations.

In the hope of escaping surgery various local astringent applications and methods of treatment have been advised, all of which are more or less futile, except in the vascular or "cyanotic" adenoid of some writers. In these cases instillations of adrenalin chloride, 1 to 5000, followed by fine sprays or vapors of mentholized albo-

lene are of service. Glycerite of tannin and other astringents can have little or no permanent effect while the underlying cause remains. Anemia, gastrointestinal derangements, or other disorders must be corrected by proper **hygiene, diet,** and **general medication** as indicated.

Internal medication offers but little. With anemic or chlorotic children one is often inclined to temporize and try to build up the system by means of **iron** and other tonics, but the speedy improvement in general condition following surgical intervention is conclusive proof that the main cause of the constitutional depression lies in the local disorder, upon which medication alone has little or no effect.

The internal and local use of iodine for its sorbefacient effect has not had success. The Bier suction hyperemia treatment, for which very temperate claims are made in hypertrophy of the faucial tonsils, does not seem to have been applied to adenoids. The tubes figured by Meyer-Schmieden for aspirating the nasal chambers and the sinuses would make but little impression in the postnasal space, although good results in atrophy of the nasopharynx are mentioned.

At one time certain "breathing exercises" were loudly vaunted as a cure for adenoids. The shallow character of respiration practised by most people and the health-giving value of deep breathing are generally comprehended in these days, especially in connection with the class of cases under consideration. Meyer appreciated the fact that a dense hyperplasia cannot be dissipated by breathing exercises, or by measures tending to promote the general health, or designed to exert a con-

tractile effect upon the morbid growth. His early essays at removal were made with a small "ring knife" passed through the anterior naris and guided by a finger inserted behind the velum. It was soon found possible to operate more easily and expeditiously through the mouth, and in consequence today the instrument shops are flooded with forceps, guillotines, and curettes designed to facilitate this procedure.

Adenoids present at birth, while never sufficiently large to endanger life, may cause obstructed nasal breathing, shown by restlessness, indrawing of the diaphragm, and inability to suck. A few days after birth the infant begins to breathe with the mouth open, to snort and sniffle. Owing to the nasal obstruction it swallows air while trying to suck, which makes it sick and gives it windy spasms.

When removing adenoids under the age of 6 months a general anesthetic is neither required nor advisable. The infant is held in a sitting position by a nurse, a small **curette** is passed up behind the soft palate into the post nasal space and brought down with one sweep. It requires but a tiny pad of adenoids to cause symptoms, but in some cases one is surprised at the amount of adenoids removed. As a rule, very little bleeding takes place. The infant should be kept warm, and if there appears to be any shock, should be given a drop or 2 of **brandy in** a little **milk.** It should not be fed for 3 hours before the operation, but can be given the breast or bottle 10 minutes or so after it. Hunter Tod (Pract., Nov., 1920).

In adopting a plan of operation the principles of thoroughness, gentleness, and celerity are to be observed. By the first is meant not a clean sweep of all the soft parts down to the bone, but a removal of projecting tabs that can be detected by the examining finger. The

second is insured by selection of instruments that include in their bite generous segments of tissue. Thus the need of frequent reintroductions is obviated and the parts are spared unnecessary violence and contusion. Finally, while undue haste is to be avoided, it is well to abbreviate as much as possible the period of narcosis. We are prone to underestimate the importance of this detail. As a matter of fact, a large proportion of accidents, both immediate and secondary, can be traced to excessive crowding of the anesthetic at the hands of one who is not expert in its management. Important among these is pulmonary abscess. General anesthesia should always be in charge of one trained for the duty, who knows how to get satisfactory relaxation with a minimum of anesthetic.

> The fatalities in a tonsil-adenoid operation may be due to: 1. Faulty administration of the anesthetic because of: (a) failure to select the appropriate anesthetic; (b) lack of knowledge, so that a deep anesthesia is mistaken for a light one; (c) failure to maintain a free air passage and to watch the respiration and circulation; (d) failure to regulate or change the anesthetic when circumstances alter; (e) overdosing, absolutely or relatively. Of these causes, (a) and (c) are more common than (e). 2. Respiratory obstruction, due to the location of the operative field just above the air passage. 3. Shock. 4. Hemorrhage.
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> Status lymphaticus should be considered as more of an idiosyncrasy; the author thinks many reported cases could have been otherwise explained. As to treatment, the head should be lowered, the face sponged with cold water, the air passage cleared, either by swabbing, maintaining firm intermittent pressure on the back of the chest, by artificial respiration, or even tracheotomy. Finger pressure over the trachea and

larynx through the skin is also suggested as a feasible means of expressing blood clots. J. D. Mortimer (Pract., xcix, 482, 1917).

Preparation of the Patient.—While **adenectomy** may not be properly considered a major operation, yet it is by all means to be postponed in the presence of any acute local disturbance, or of concurrent general disorder, or when an epidemic of any contagious disease is prevailing. The advice once given by Lennox Browne to operate during an attack of diphtheria, with a view of averting the necessity of a tracheotomy, is refuted by the modern mode of treatment in that disease. Locally an attempt to secure an aseptic operative field by the use of antiseptics is hopeless. The parts should be cleansed of secretion by douching with warm **normal salt solution**, but anything beyond that is superfluous. Large faucial tonsils which interfere with manipulations should first be excised.

> Local application of Hess's **thromboplastin** recommended as a preventive of post-operative hemorrhage, on the basis of 2036 adenoid and tonsil operations. J. J. Cronin (Jour. Amer. Med. Assoc., lxvi, 557).
>
> Practically all the acute infectious diseases of childhood have followed adenectomy. The writer warns against operating in the presence of local infection or during epidemics. Much thought has been given to the reasons for unexpectedly slow and limited improvement of the patient in some instances of adenectomy, especially as regards mouth breathing. W. E. Grove (Johns Hopkins Hosp. Bull., Apr., 1913).

Bleeders should be avoided, or prepared by a few doses of **calcium chloride or lactate**. The strange conflict of opinion, both in the laboratory and the clinic, as to the effect of calcium

upon the coagulability of the blood
tends to weaken confidence, but pos-
sibly should rather teach us to use it in
larger doses than has hitherto been
the custom. The weight of evidence is
strongly in favor of calcium lactate,
some authorities asserting that the chlo-
ride is practically inert (W. K. Simp-
son). The former is more agreeable to
take, and thus far no unpleasant con-
sequences from larger doses have been
experienced.

> Clinical experience shows that **cal-
> cium lactate** has a controlling influ-
> ence in hastening the coagulation of
> the blood. Its efficacy is more
> marked in hemophilic cases where
> the coagulation is delayed than in
> cases of normal coagulation time.
> Before operation, especially on ton-
> sils and adenoids, careful inquiry
> should be made relative to any hemo-
> philic heredity or tendency. In sus-
> picious cases the coagulation period
> should be determined before opera-
> tion. It is questionable, if not posi-
> tively contraindicated, whether such
> operations should be undertaken in
> hemophilic cases other than under the
> most extreme urgency. In all cases
> of operation for the removal of ton-
> sils and adenoids, calcium lactate
> should be given for a period prior to
> and after the operation, both for its
> possible effect in diminishing the im-
> mediate hemorrhage and in prevent-
> ing secondary surface hemorrhage.
> Of the calcium salts, the lactate is
> more positive in its results, is more
> agreeable to administer, and is less
> irritating to the stomach. Simpson
> (Medical Record, Sept. 25, 1909).

> The writer submits the following
> hints on the tonsil-adenoid operation
> based on an experience of 5000 cases:
> 1. In middle suppuration, always ex-
> amine for adenoids. The same rule
> holds good in the familiar fleeting
> acute catarrhs of the middle ear. 2.
> In acute suppuration of the middle
> ear do not operate on the throat until
> the acute ear symptoms have sub-
> sided. 3. Before operating make sure

> that the mouth is reasonably clean.
> 4. Avoid passing the finger into the
> nasopharynx after the operation has
> been finished. If it is necessary, use
> rubber gloves. 5. Severe tonsillar
> hemorrhage, though often termed re-
> actionary or secondary, is seldom
> either. It is usually primary. 6.
> After all operations on the nose or
> throat, the patient, no matter what
> his age, when put back to bed should
> not be allowed to lie on his back.
> He should be laid semiprone on his
> side with face turned half-down, and
> with a basin or bowl under the mouth
> and nose. 7. Always visit the patient
> not later than three hours after the
> operation. 8. When about to examine
> the bleeding throat of a conscious
> patient, first of all insert a mouth-
> gag. 9. No case of deafness can be
> considered properly examined with-
> out the nasopharyngoscope. D.
> McKenzie (Pract., Aug., 1917).

The bowels should be evacuated by
a **saline laxative** and no solid food
and no milk given for at least six
hours beforehand.

Position of the Patient.—The *erect*
position is advocated by some, because
it is that to which we are accustomed
in routine work, the loss of blood is
less, and *débris* and blood tend to escape
forward rather than backward toward
the glottis. Moreover it is thought that
the ears are in less danger as a result of
freedom from accumulations at the
openings of the Eustachian tubes. The
position *on the side* is favored by others
on account of the tendency of blood
and secretions to gravitate to the de-
pendent side and drain off through the
nose and mouth.

After all has been said, the *recumbent
position* seems to be the most convenient
for all concerned and is free from risk,
provided the anesthesia be not profound
and the reflexes are preserved. In such
case foreign material approaching the
larynx is promptly ejected, and what

finds its way into the stomach is thrown up before complete recovery from the anesthetic. With attention to this point, the so-called Rose's position, the head being dependent, is not essential.

> When the operator selects the recumbent position, the body should be horizontally on the back, the head being neither flexed nor extended. With the head extended the cervical curve of the spinal column is increased. In this position the operator is liable to cut deeply into the structures of the posterior pharyngeal wall, which will be stripped down by the curette. A lateral position favors the drainage of blood from the pharynx and in no way inconveniences the surgeon in removing the tonsils. For the latter purpose a small guillotine is better than a large one, and is not so liable to slip. F. C. Carle (Lancet, May 13, p. 1265, 1905).

Anesthesia.—In children under one year the adenoid growth is so soft and friable that it can be readily broken down with the fingernail and no anesthetic is necessary. An artificial nail adjusted to the fingertip (Creswell-Baber, Motais) has no advantage over a curette, and rather hampers freedom of manipulation. Local anesthesia with **novocaine, apothesine, cocaine, stovaine,** or **alypin** is reserved for adults and for children old enough to be manageable.

> The writer advocates local anesthesia, describing its advantages over general anesthesia as follows: With local anesthesia there is less danger of starting up an old tuberculous lesion of the lungs, which occurs so frequently when general anesthesia is universally employed. General anesthetics have been known to produce nephritis, cardiac and respiratory failure, and insufflation pneumonia. No cases of abscess of the lung have been reported following tonsillectomy under local anesthesia. It is available when general anesthesia is contra-indicated, as in chronic nephritis, respiratory disorders, pulmonary tuberculosis, etc. Local anesthesia has an advantage in the rapidity with which the operation may be done without the shock which follows a general anesthetic. When the case is uncomplicated, local anesthesia is a time-saver and requires fewer assistants.

> Local anesthesia is contra-indicated in children under 10 years of age, in secondary operations, when there have been repeated attacks of peritonsillar abscess, and in highly neurotic adults or those with extremely sensitive throats. One-half per cent. **novocaine (procaine),** with 1 drop of $\frac{1}{1000}$ **adrenalin** to each dram (4 Gm.) of the anesthetic, is preferred, 1 dram of the mixture being injected between the capsule and muscle of each tonsil. The same solution is used for adenoids. F. O. Lewis (Therap. Gaz., xliii, 328, 1919).

> The writer advocates the use of **nitrous oxide** anesthesia in the removal of tonsils and adenoids in children less than 14 years of age. In older patients **cocaine** and **procaine** are used. Yorke (Brit. Med. Jour., Aug. 28, 1920).

Although certain statistics, like those given by C. A. Parker, from Golden Square and St. Bartholomew's Hospitals, are partial to chloroform, it is the general belief that this agent is especially dangerous in lymphatism and should never be used (F. W. Hinkel). The danger is said to be less when it is joined with oxygen. **Nitrous oxide gas** is universally admitted to carry the least risk, but it is too transient for any but the simplest case. Combined with **oxygen,** its effect is slightly more prolonged and in other respects it is satisfactory (W. E. Casselberry). When used as a preliminary to **ether** in what is known as the *gas-ether sequence,* with a Ben-

nett inhaler, the process of narcosis is rendered as agreeable, rapid, and safe as possible. By this method a much smaller quantity of ether is needed with proportionate reduction in stimulation of mucous secretion and less of unpleasant after-effect, two of the chief objections to ether. Braden Kyle quotes Royer to the effect that secretion is lessened by adding to the ether a few drops of **oil of Hungarian pine.** The disagreeable odor of ether may be partially prevented by first pouring a little cologne water in the mask, and thus the confidence of a timid patient may be secured. By many operators the "drop" method of giving ether is preferred, especially in young children, and thereby the strain upon the chest walls incident to the use of a closed inhaler is avoided. By some the use of **morphine, atropine, or chloretone** to reduce mucous secretion is advised, but this is not to be recommended in the very young. A clear operative field may be procured by means of some form of suction device, now so generally in use.

Those who oppose general anesthesia refuse to admit the fact that the shock without it, especially in a nervous child, overbalances any risk incurred when the plan just outlined is pursued. It is almost indispensable when, as often happens, the palatal tonsils must be removed or other instrumentation done at the same time.

Ethyl bromide and ethyl chloride, the latter said to be the less objectionable, have no supreme advantage and are not free from risk. According to Lermoyez, the difficulty in regulating the dose of ethyl chloride, owing to its great volatility, is overcome by giving it with a suitable mask, whereby the quantity inhaled is precisely known. The Apperson inhaler is highly recommended, from 3 to 5 grams of the anesthetic being required for a short operation. The drug is so rapidly eliminated that after-effects are few or absent. Other good features claimed for it by those experienced are ease of administration and rapidity of action. It may be given prior to other anesthetics, or alone continuously for an indefinite time without regard to the position of the patient, upright or prone (G. F. Hawley).

At the Royal Infirmary of Edinburgh, the experience of T. D. Luke has been so gratifying that he recommends ethyl chloride as a matter of routine for short operations. On the other hand Z. Mennell, at St. Thomas's, London, notes the frequent occurrence of pulmonary embolism at that institution since the introduction of ethyl chloride. He attributes it to increased coagulability of the blood caused by the drug, and on this account has abandoned its use. Those who advocate ethyl bromide ascribe disasters with it to the use of an impure product, or to the mistake of having substituted for it ethylene bromide. In addition we are enjoined to give it *en masse,* admitting no air, and to continue the administration no longer than one minute (A. R. Solenberger). Most operators will find sixty seconds too short a time for thorough work.

The **Schleich inhalation mixture** (E. Mayer) and the **A. C. E. mixture** are urged by some, but have no special attraction.

If the operation is to be done in the upright position, it is customary to give the anesthetic to the patient lying down and to slowly elevate the

body when all is ready. Special operating chairs have been devised for this purpose (T. R. French).

The question of safety being of the first importance, too much stress cannot be laid upon the necessity of choosing a reliable anesthetic and a trustworthy anesthetist, and **ether** or **nitrous oxide-oxygen ether** is the safest and the anesthetic of preference if general anesthesia is used.

Insufflation anesthesia, or the forcing of ether vapor to the lungs through a tracheal tube (Jackson direct laryngoscope), is pronounced by C. A. Elsberg, of Mount Sinai Hospital, who introduced the method and devised an excellent apparatus for the purpose, "ideal" in operations in the upper air tract, as regards prevention of aspiration of blood and mucous and as to rapidity and safety of narcosis. This view is confirmed by C. H. Peck from experience with a number of cases at Roosevelt Hospital.

> **Gas and oxygen** passed **over anesthol** for the induction of anesthesia, and **gas-oxygen-ether** to maintain it, are employed by the writer in adenoid and tonsil work. His equipment consists of an electric heater for warming the anesthetic and a vapor mask with Sanford nasal tubes or a mouth hook and a Whitehead self-retaining mouth gag. Anesthol is placed in one bottle of the ether attachment, and ether in the second bottle. The induction is begun with nitrous oxide and oxygen, and after 15 to 30 seconds the anesthol is turned on gradually. In from 1 to 3 minutes the third stage of anesthesia is reached, usually without a struggling stage. The ether is then turned on very gradually. When the patient is able to breathe gas-oxygen-ether without coughing or hesitation in breathing, the anesthol is turned off and the anesthesia continued with

gas-oxygen-ether. The patient's skin remains pink throughout the procedure and there is no rise in blood pressure. In children up to 6 years of age the ether may be turned off very shortly after the operation is begun, the induction of the anesthesia being carried through with gas oxygen only, or the gas may be turned off and the anesthesia continued with ether and oxygen. When the adenoids are being removed the nitrous oxide and the ether are turned off and oxygen is given, the blood being thus in the best possible condition for coagulation. G. T. Gwathmey (N. Y. Med. Jour., cxi, 1065, 1920).

Instruments and Methods.—Chemical caustics and the electric cautery have been generally superseded by instruments for extracting the morbid tissue instead of destroying it and allowing it to slough away.

Caustics are available, if ever, only in tractable patients and under guidance of the rhinoscopic mirror, the palate being held forward with a retractor (White) or by means of elastic ligatures (flexible catheters) passed through the nares and out of the mouth, the nasal and buccal ends being tied or clamped together. Under **cocaine** the process is not extremely painful. **Silver nitrate** and **chromic acid** have been used in this way. Without the utmost care and the use of a guarded applicator there is danger of excessive damage and violent reaction. The **electric cautery** point or loop is more precise and manageable, but at best these methods are tedious and unsatisfactory. They are reserved for hematophiliacs and those who refuse to be cut. In other cases the cold-wire snare, the guillotine, forceps, and the curette provide a wide choice of cutting instruments. A straight **snare** (Jarvis) may be passed through the naris, or a curved one behind the

velum (Bosworth). It is successful only when the lymphoid tissue is so bunched in the vault that the wire can readily encircle its base. It is apt to slip and include only superficial portions.

The **guillotine** method, or the combined **guillotine-curettage**, or the **guillotine-forceps** methods are the most commonly used at present.

The variations of instruments of all types are numerous, the main features of each type, however, being similar.

The guillotine type in common use is the La Force or some modification, and in the average case, removal of adenoids by this method proves safe and satisfactory.

The early instruments for scraping were the sharp spoons of Justi and of Trautmann. **Curettes** are now made larger and of different sizes and shapes, and some are provided with forks to catch the resected fragments. Such complicating attachments are a disadvantage rather than otherwise. The simpler the instrument, the easier it is to handle and keep aseptic.

While the anesthetic is being given, the patient lies flat on the back. After

White's palate retractor.

the muscles are somewhat relaxed, a mouth-gag is inserted. If the palatal tonsils are enlarged, they are first removed. A little more anesthetic may now be required. The nasopharynx is explored with the finger to determine the extent and distribution of the growths.

The instrument of choice is thereupon inserted behind the soft palate and velum, pressed firmly upward and backward into the vault of the pharynx and, if the guillotine type is used, the blade is forced shut and the adeno-
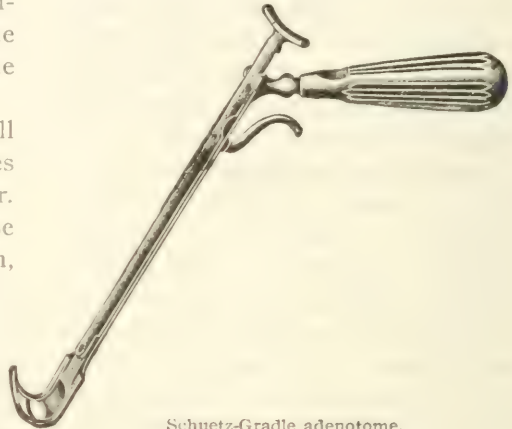
Schuetz-Gradle adenotome.

tome removed with a sweeping motion. Digital examination of the pharyngeal vault following removal of the main mass of adenoid tissue by this means may disclose small shreds remaining, especially in the region of Rosenmueller's fossæ, and these may be removed by some form of curette or forceps, as the individual operator prefers.

By many a curette of the Gottstein or Beckmann pattern is used for the whole operation. A curette of proper shape and size, and correctly used, certainly sweeps off the tissue most effectually. The blade, always quite sharp, is slipped behind the velum and crowded from below upward close to the posterior margin of the vomer, and then by a quick movement pushed backward and slightly downward through the base of the growth. A clean, complete removal is thus ensured, at least as to the vault itself, when the conformation of the region is normal. Unless the

blade is passed close to the posterior surface of the velum and is made to hug the vomer in its upward movement, pendent masses are apt to be crowded into the choanæ. By giving the shaft of the curette a curved or bayonet shape it is possible to avoid the obstacle offered by the incisor teeth or by the palate and thus reach farther forward in the vault (J. Fein).

part is apt to remain vulnerable for some time, often highly sensitive to atmospheric changes, so that the attacks may not altogether cease until steps have been taken to brace up the relaxed mucous membrane and reduce its susceptibility to chills. It is, therefore, advisable to remove the patient, soon after the operation, to the seaside, choosing a situation which is moderately bracing, but not bleak. He should be taught to breathe as much as possible through the nose, and should pass the greater

Denhard's mouth gag.

Other curettes are made heart-shaped, so as to actually enter the nares on either side of the septum (C. E. Munger).

The nasal route for reaching adenoids has been revived by Freer, who

part of his time in the open air. There are two applications which are very serviceable in these cases. Twice a day a solution of **resorcin in normal saline** (5 or 10 grains to the ounce, with the addition of half a dram of tincture of **hamamelis)** should be in-
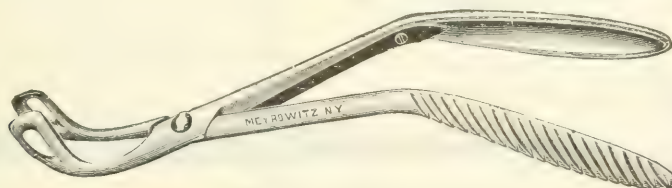
Brandegee's adenoid forceps.

recommends for the purpose a modification of Ingal's straight nasal cutting forceps. The blades are directed by the finger passed behind the velum, and in any case it is a useful instrument for clearing out the postnasal arches, where fragments are sometimes missed and afterward give trouble.

Even when the postnasal adenoids have been completely extirpated, the

stilled into the nostrils as the child lies on his back with his head supported by a pillow. Five or six drops may be used to each nostril with a "dropper," allowing the fluid to trickle down into the pharynx. After using these drops for a week we can begin to paint the pharynx. The best application for this purpose is a solution of 15 grains of **potassium iodide** and 12 of **iodine** in an ounce of water, well sweetened with **glycerin.** This should be applied twice a day to the

pharynx with a brush, taking care to sweep the brush round with a turn of the wrist before withdrawing it, so as to reach as high up as possible behind the soft palate. This application not only checks morbid over-secretion by curing the nasopharyngeal catarrh, but also puts an end to laryngeal irritation and favorably influences the glandular enlargement. In fact, this is the very best method

treatment does cause shrinkage of tonsils and adenoids and an increased fibrosis and an atrophy of the lymphoid constituents of these structures, but whether the diseased process is arrested—and this and not size is the usual indication for treatment or removal—remains to be proven, in view of the divergence of opinion.

Knight's adenoid forceps.

of treatment for acutely swollen cervical glands, and as long as the latter remain of elastic softness, varying in size from time to time according to the amount of laryngeal worry, we may expect them to be dissipated by this means. Smith (Practitioner, Jan., 1910).

Recently, much has been done and much has been reported regarding the treatment of diseased tonsils and adenoids by means of **X-ray** and radium.

The author's experience has been that but little, if any, change has been produced in the diseased condition and operation has been necessary in many cases which have previously been exposed to X-ray or radium treatment.

The chances of recurrence in the ordinary case diminish rapidly from the age of 4 to 7 after which they are practically *nil*, unless anterior nasal obstruction exists or measles or whooping-cough supervenes. T. Guthrie (Lancet, Apr. 20, 1912).

Gottstein's adenoid curette.

Many of the adherents of these methods have made claims of remarkable results and have advocated treatment by such means instead of surgical removal.

The opinions of the writers for and against this method are so divergent and so numerous that the conclusion must be reached that these methods of treatment are still on trial.

Undoubtedly X-ray or radium

Accidents and Complications.—The most serious accident is hemorrhage, which may be first shown by pallor and rapid, flickering pulse. Small children should be closely watched and not allowed to sleep continuously for several hours after operation. The contrast between the quiet and the previously noisy breathing often creates enough anxiety to enforce this caution. Bleeding usually ceases spon-

taneously in a very few minutes. The total loss of blood is difficult to estimate; according to C. G. Coakley, from 2 to 8 ounces is the ordinary quantity. If in excess or too long continued, measures to check it must be adopted.

Operations upon the pharyngeal tonsils are generally considered without danger, yet wound infection and hemorrhage, although comparatively rare, do occur frequently enough to warrant careful attention. Hemorrhages may be divided into 2 types: those appearing at the time of operation, and those occurring some time afterward.

In the first instance the causes lie in a constitutional or a local condition, the most important of which is hemophilia. This is shown by family and personal history. If there exists absolute proof of a hemophilia, naturally the operation would be denied. But in such cases as appear relatively doubtful the operation should be given the benefit of the doubt. An unrecognized leukemia can be the cause of excessive hemorrhage. Characteristic is the livid bleached color of the tonsils. Operation in such cases can produce the same untoward results as in hemophilia. Among other diseases which impose the danger of severe postoperative hemorrhage are nephritis, heart lesions, etc., which, however, appear so rarely in cases needing adenoidectomy that they can be neglected.

Many authors have associated severe postoperative hemorrhage with the coincidence of the operation and menstruation. About 1 per cent. of cases have postoperative hemorrhage. Injury to neighboring parts, and especially the leaving of partly removed tissue shreds, are the important factors. The former more often leads to hemorrhage immediately following the operation, and only to afterbleeding when the blood-clot covering the lesion is accidentally removed.

Mucous membrane shreds hanging from the wound are found in over 50 per cent. of after-hemorrhages. Hemorrhages occurring after several days generally follow sudden muscular exertion, such as sneezing, blowing the nose, etc., and are due to dislocation of the exudate covering the wounded surface. Healing had progressed so far after a week's time that bleeding is no longer to be feared. Haymann (Archiv f. Laryngologie, Bd. xxi, S. 15, 1908-1909).

Reference has already been made to the internal use of **calcium chloride** or **lactate** in hemophilia, and many local applications are advocated such as **thromboplastin, hemoplastin, coagulen,** and **thrombokinase.** Locally, instillations of **adrenalin chloride,** 1 to 1000, are sometimes effective. Direct pressure by means of a **gauze tampon** crowded up into the vault in the grasp of a postnasal forceps is usually successful. At times it may be necessary to retain the postnasal gauze tampon *in situ* for several hours, having pulled it up firmly in the vault of pharynx by means of tape through nostril and securing tape externally by means of adhesive plaster. The gauze may be soaked in a saturated solution of **tannogallic acid** (1 part gallic, 3 parts tannic), one of the cleanest and most active hemostatics. Signs of collapse are to be combated by saline injections, stimulants, constricting the extremities, and similar expedients. Even after extreme exsanguination the repair of waste is generally rapid, but may need to be encouraged by the use of **ferruginous tonics** or other medication.

Such being the case, the proposal of Iglauer to transform **adenectomy** into an "almost bloodless" operation by packing the postnasal space with a tampon of rubber sponge the moment

the adenoid mass has been removed is of doubtful utility.

The plan suggested is like that followed in plugging the posterior nares for epistaxis.

The tampon is ready before the operation is begun, and the tape attached to it is used as a palate retractor during instrumentation.

The handle of the forceps cutting laterally should not be too much depressed lest the margin of the vomer be nipped between the blades. Care should be taken to keep the blade of a cutting instrument in the middle line of the vault: if tilted to one side, there is danger of harm to the Eustachian cushion.

A rare and interesting complication, torticollis, has been described by several writers and is probably due to sepsis or to excessive energy in the use of instruments. It disappears spontaneously in a few days and is worthy of note only because of the unnecessary alarm to which it may give rise.

Laceration of the velum would seem to be inexcusable, but has been known to occur with rough handling of an excessively large instrument, or from attempting to make use of a cutting edge in a struggling child, or before one is quite sure that the instrument has passed beyond the plane of the velum and is well within the cavity of the nasopharynx. Finally, the mucous membrane may be stripped up over an excessive area, if too dull an instrument be used, or if it be forced too deeply into the tissues. With the exception of the first-mentioned, hemorrhage, these accidents are obviously all unfortunate results of faulty manipulation.

Reports of deaths from pulmonary abscess following operative procedures of the upper respiratory tract have been increasingly numerous and have stimulated investigation of this complication, and have added many adherents to the view held by too few, unfortunately, that operations in this area are not to be seriously considered.

There is still a wide divergence of opinion as to whether the condition is a result of blood stream infection, of lymph channel transmission, or of direct inspiraton during operation, and each investigator holds his own view regarding the means of production and of the methods and the appliances for possible prevention of this complication.

Attention has been called by Wyatt Wingrave and others to a peculiar transitory rash resembling that of scarlatina at times following removal of adenoids or tonsils. It merits notice only for the danger that it might be confounded with a more serious infectious exanthema. No precise theory of the phenomenon is propounded, whether septic or nervous, although marked leucocytosis is demonstrable for a week or ten days after. Several cases of alleged sepsis have been recorded, but in many the histories are by no means conclusive. A case of fatal meningitis, believed to be septic, has been reported by Shurly; two similar cases have been noted by Putnam, who expresses the opinion that such sequelæ are not uncommon. An interesting case of cavernous sinus thrombosis in which the surface of the basilar process of the occipital bone had been shaved off together with an adenoid mass with a Beckmann curette is a graphic warning against the use of extraordinary force (A. E. Wales). Cases of pharyngeal

abscess, inflammation of the cervical glands, endocarditis, and acute rheumatism have been met with by various observers after adenectomy.

Several instances of lighting up of latent tuberculosis by adenectomy have been reported (Lermoyez, Chappell). It is perhaps more correct to say that tubercle bacilli lying in the operative field have ready admission to the circulation through the divided lymph-channels, whence general infection follows. In the majority of cases the adenoid tuberculosis is undoubtedly *secondary* to a focus in the lung or elsewhere which is excited to activity by the surgical shock of operation. In a *primary* case the results of removal are favorable (E. H. White), but there must always be difficulty in deciding this question of priority.

> In the development of pulmonary tuberculosis adenoids may sometimes be direct channels of infection, but their importance is probably more often indirect by predisposing to catarrhal inflammations of the upper respiratory tract. E. Hamilton White (Amer. Jour. Med. Sci., Aug., p. 228, 1907).
>
> The writer found evidences of tuberculosis in the growths in only 1 of 27 cases of adenoid vegetation, and in this case it was evidently secondary. Wikner (Hygieia, April, 1910).

An interesting case is mentioned by J. L. Morse, in which "adenoids were removed from an infant of five months during the early stage of tuberculous meningitis, tubercle bacilli being found in the adenoid tissue." The possibility of infection by this route is looked upon as a strong reason for operating in the early months of life, even with the certainty that a repetition will be called for at a later period.

Spasm of the glottis requiring **tracheotomy,** as in cases of his own, is believed by Holger Mygind to be not infrequent in adenectomy without anesthesia in rachitic children, and one should be prepared for such an emergency.

> The writer has twice witnessed serious disturbance of respiration (laryngospasm with stridulous inspiration and marked cyanosis of the lips) as a result of **adenotomy** without use of chloroform. Both cases were children under 2 years having symptoms of rachitis. In the third case, in a boy of 2 years, with rachitic deformities, there was sudden collapse accompanied with suspension of respiration and cyanosis consequent to adenotomy, which required **tracheotomy.** The child's mother later declared that the child was subject to fits of suspension of respiration with cyanosis. On two occasions he had such attacks in the presence of the family doctor, and artificial respiration had to be employed. Holger Mygind (Hospitalstidende, Nov. 18, p. 1173, 1903).
>
> Case in which a very large adenoid removed from a child aged 6 years gave rise to asphyxia on spasmodic closure of the jaw just as the child was apparently under complete ether anesthesia. The writer had to resort to **artificial respiration, hypodermic injections, forcible opening of the jaw,** and traction of the **tongue** in order to resuscitate his patient. G. L. Richards (Laryngoscope, Feb., p. 289, 1905).

After-treatment. — The control of hemorrhage, and that in very exceptional cases, is practically the only indication for interference during convalescence. If catarrhal secretion is overabundant, it is sometimes desirable to keep the parts clean with a douche or coarse spray of warm **normal salt solution.** Drainage from this region is so good that sepsis is almost unknown, and it is well to abstain from the use of antiseptics, either in solution or powder. In order to prevent the formation of adhesions, the passage of the finger into the vault for a few days after

operation has been recommended. Although no statistics on this point are available, it is believed that adventitious bands met with in adult life are due not to operative interference, but to attrition and erosion of lymphoid masses in childhood which have been neglected and have finally undergone spontaneous shrinkage.

> Removal of adenoid vegetation has brought about, in the writer's hands, recovery of 2 cases of exophthalmic goiter, 1 of glaucoma due to lesion of the fifth pair and not relieved by iridectomy, and of 1 case of Addison's disease. The persistence of the craniopharyngeal canal and an accessory pituitary gland encountered sometimes in the pharynx, might cause an alteration in the secretory function of the pituitary body, and the sympathetic nerve, through the other glands of internal secretion. Popp (Annales des mal. de l'oreille, du larynx, etc., Oct., 1909).

> The pharynx, as a rule, is relatively small in children with adenoids, sometimes interfering with respiration, deglutition, and clear speech after the adenoids have been removed. It is possible in such cases to develop and broaden the bony pharyngeal walls by **exercises of** the **pterygoid muscles,** viz., lateral, verticle and anteroposterior movements of the lower jaw, made against resistance offered by the hand of an instructor who holds the jaw firmly. F. Warner (Lancet, Dec. 20, 1913).

No procedure in the upper air tract has added so much to the vigor of the race as **removal of adenoid vegetations,** and the fact must be admitted that they are often a source of disease, even when their volume is not sufficient to cause obstructive symptoms.

CHARLES H. KNIGHT,
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AND
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ADIPOSIS.   See OBESITY.

ADIPOSIS DOLOROSA; DERCUM'S DISEASE.

[The term "Dercum's disease" is that by which adiposis dolorosa is generally known in Europe. Hence its introduction here by the Editors.]

DEFINITION.—Adiposis dolorosa derives its name from its two principal features, namely, fat and pain.

[Objection may naturally be made to the form of the word "adiposis," as it is of mixed origin, being made up of a Latin root joined to a Greek termination. It has, however, the sanction of generations of use among English-speaking writers, and, besides, is paralleled by other mongrel words in common use, such as terminology, which no one any longer questions. The correct Latin form of the word would, of course, be "adipositas," the word used by German writers. However, adipositas is equally a coined word, a word artificially made, for it is not used by any Latin writer. The real Latin is "obesitas," which, as purists, we ought to use. F. X. DERCUM.]

In 1888, the writer described the symptoms which constitute this affection in reporting a case under the title of a subcutaneous connective-tissue dystrophy. Later, in 1892, he grouped this case, a second described by F. P. Henry, and a third discovered in the wards of the Philadelphia General Hospital under the name "adiposis dolorosa," by which the affection has since become generally known. Within the next few years cases were published by Collins, Peterson, Ewald, Eshner, Spiller, Féré, and others. In 1901, Louis Vitaut (Thèse de Lyon, 1901, "Maladie de Dercum") published a special treatise on the subject. His description of the affection was so full and accurate that at the present date it needs but little modification and but few additions; the latter mainly bear upon the pathology of the affection. Up to the present

time between 50 and 60 cases have been recorded. [Among the more important papers upon the subject are those of Frankenheimer (Jour. Amer. Med. Ass'n, 1908, i, p. 1012), of Price (Amer. Jour. Med. Sci., May, 1909), and the thesis of Poirier, Montpelier, 1910.]

SYMPTOMS AND COURSE.— The development of the disease is usually slow and insidious. A woman who, up to the period of onset, has been well and occupied with her usual occupation notices a slight pain or tenderness in this or that portion of the body. This early symptom of pain is very variable in character and in intensity. Most often it is a sensation of smarting or stinging more or less annoying because of its persistence. Sometimes the pain, even in the beginning, is severe, though this is unusual. At other times the onset of symptoms is preceded by a sensation of cold in regions in which pain subsequently makes its appearance. As a rule, the pains at first are not very pronounced and the patient is for some time able to follow her ordinary occupation. Furthermore, the pains are not persistent, but recur at intervals, the patient being comfortable for hours and sometimes for days at a time. Little by little the pains become more pronounced, they increase in intensity and are then also accompanied by distinct local changes. The patient naturally examines the part which is painful and may note these changes herself. Sometimes there is a little flushing of the skin and sooner or later a swelling is noted. At first it is hardly appreciable, but gradually becomes more pronounced. The swelling may give a sensation to the finger of a rather firm localized edema. As a rule, it is in the beginning a small nodule,—smaller than a walnut, rarely larger. Sometimes a number of such swellings are noted at the same time. The affection continues to evolve, usually slowly; the pains become more intense and more frequent, and gradually the tumefactions change their character and finally become veritable tumors or great tumor masses. In rare cases the fatty deposit appears to make its appearance without either previous or concomitant pain, the pain making its appearance only after the enlargements or swellings have existed for some time. This, as already stated, is unusual, the most common history by far being that just outlined.

The pain is quite commonly paroxysmal, though in long-established cases it may be continuous. In the intervals the tumefactions are usually tender or painful to pressure.

When the disease is well established, we may distinguish, as pointed out by Vitaut, 4 cardinal symptoms, namely, tumor formations, pain, asthenia, and psychic symptoms.

The swellings may present themselves under three different aspects. Sometimes they are small, of variable dimensions, distinct from one another, and readily isolated. Under these circumstances they present what Vitaut has termed the nodular form of the disease. Sometimes they form extensive masses, invading an entire limb or the segment of a limb. To this condition Vitaut has given the name of "localized diffuse form." Finally, a tumor, properly speaking, may not be present, but the entire body may be augmented in volume in consequence of a hyperplasia of the fatty subconnective tissue. This condition Vitaut has called "the generalized diffuse form."

The Nodular Form.—The nodular form manifests itself at first by pains,

variable in character, stinging, itching, smarting, shooting, soon followed by a slight redness of the skin and a slight induration scarcely appreciable to the finger. If we examine the painful area, we feel a tumefaction, usually of small changes, so that it no longer has the appearance of a simple tumefaction, but that of an actual tumor. Each increase of swelling is preceded or attended by characteristic pains. The latter are sometimes so sudden in their onset and

Author's first case   (*Dercum.*)

size, at first yielding and later a little more resistant. The sensation is that of a firm edema, which is not well differentiated from the surrounding tissue. The tumefaction appears to develop slowly in keeping with successive attacks or crises of pain. Gradually it becomes somewhat better defined, its volume increases, and its consistence so severe as to cause the patient to cry out. During the height of the paroxysm, the tumor may resemble very closely, in the sensation which it gives to the fingers, a "caking breast." The painful crisis having passed, it is found that the dimensions of the swelling have distinctly increased. It has become permanently larger, as well

as more resistant and better defined. After repeated paroxysms, the swelling resembles a distinct tumor more and more closely. In certain portions, the mass may appear finely lobulated, while in other parts it gives to the fingers the capsulated. Sometimes after a crisis we discover around the tumor a well-defined edematous zone, which in subsequent crises undergoes a transformation such as the original mass itself had undergone. In this way the mass may
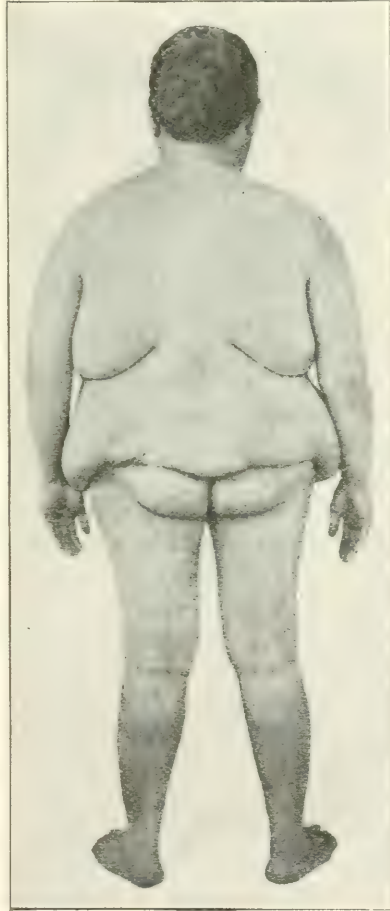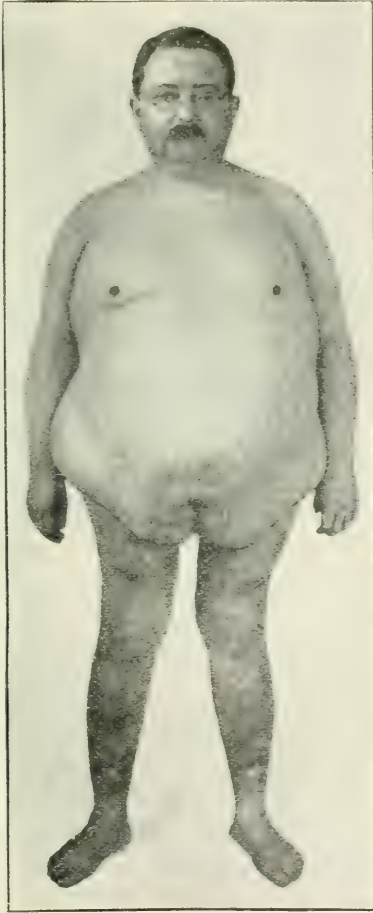
Case of adiposis dolorosa in a male. (*Dercum.*)

sensation of a bag of worms beneath the skin. Each painful crisis leaves behind it very appreciable changes. In an area where nothing existed previously, we find after a crisis a diffuse edematous tumefaction; if the tumefaction has existed previous to the crisis, we find it transformed into a lobulated tumor more or less well encapsulated eventually attain great size. The various stages of the evolution of these masses can be followed very closely by palpation. One and the same patient, besides, usually presents in various regions tumors in various stages of development.

Painful crises supervene usually without appreciable cause; at times they are

provoked by trauma and at others they ensue upon unusual exertion. The patient is frequently very positive in stating that slight contusions of the surface or that excessive fatigue provokes the painful crises.

The tumors are, of course, variable in size. Some of the very smallest may be no larger than a pea, though so small a mass is the exception. More frequently the mass is of the size of a walnut or a small orange. Much larger sizes are met with. The larger masses are of course evident to ordinary visual inspection; the smaller ones require to be sought for by palpation. If we examine the patient attentively in a good light, we are struck by the changes in the skin in certain areas. In places, indeed, it presents a bluish tint due to a slight superficial veining, and if we examine such a region by the feel we frequently discover a small subjacent tumor. Small as the tumor may be, it may betray its existence by this bluish tint in the skin which covers it. It happens sometimes that these small tumors become confluent and finally form a single large mass. Such a mass gives rise to a sensation like that of a varicocele or of a bag of worms.

The masses do not appear to have a special localization; they are sometimes symmetrical in the beginning, but soon group themselves without any apparent order. They develop by preference over the limbs or in the segments of a limb. In some patients it is limited to the arms and thighs, or forearms and legs in others. Sometimes we find them on the thorax, abdomen, and lumbosacral region. The face, hands, and feet are never involved.

The relations of these neoplasms to the surrounding tissue vary according to the degree of their development. In the state of edematous swelling, they pass without exact limitation into the surrounding tissue. The skin is but slightly movable over them. Later, when they form distinct tumors, more or less encapsulated, they are mobile in all directions and the skin which covers them may be folded above them. However, they are slightly adherent to the latter, so that if one tries to displace the superjacent skin the movement is transmitted to the underlying tumor. Finally it may be noted that these masses are painful not only during the crises, but are very tender to pressure, and this tenderness, as already pointed out, may persist in the intervals between the paroxysms.

The Localized Diffuse Form.—The localized diffuse form may present itself primarily or it may develop out of the nodular form. When it develops from the nodular form, it is because the nodules multiply so rapidly that they unite and become confluent. In this way a more or less voluminous mass may develop, which involves a portion of a limb or it may be a segment of a limb or even an entire limb. However, this is not the usual method of origin of the localized diffuse form. In the nodular form the separate masses are generally so small and the evolution so slow that the patient has usually been under observation for some time before the masses become confluent. More frequently the localized diffuse form originates spontaneously and rapidly in an entire limb or a segment of a limb. In such a case the pains are felt over a correspondingly extensive region. At first the entire region presents an edematous swelling easily observable by the eye. Subsequently the evolution of the mass is substantially the same as in the nodular form. Painful crises are

here again present and the swelling increases in size with each successive attack. Finally, a mass is formed which is resistant and painful to pressure. It may be quite smooth or it may be finely lobulated, or separate, apparently encapsulated tumors may be found imbedded in the general lipomatous mass.

Naturally, in the localized diffuse form it is difficult to make out the limitations as clearly as in the nodular form. The masses involve more especially the limbs, excluding save in the rarest instances the hands, the feet, and the face; not rarely they are found on the thighs and on the back. The tumefaction may be excessively painful and may present during a crisis the sensation given by a breast distended by milk or, to repeat a term already used, a "caked breast."

The Generalized Diffuse Form.—The generalized diffuse form is much less characteristic than the nodular or the localized diffuse form. The origin and course of the affection is, however, the same. The edema may appear rapidly, even suddenly, over the greater part of the surface of the body and limbs, exclusive again of the face, hands, and feet. It increases progressively and produces a general lipomatosis. More frequently it begins in a certain part, such as the abdomen, sometimes upon one side, and then diffuses itself gradually over neighboring portions of the trunk and limbs. Other masses may make their appearance at the same time or subsequently, and, becoming confluent with the original mass and each other, a diffuse lipomatosis results. The regions affected are ordinarily the arms, the chest, the abdomen, the hips, and the thighs. Contrary to the case in the nodular and localized diffuse forms, the hands and feet are not always in this form absolutely free. At an advanced stage of the disease, it is not unusual to see small masses of lipomatous tissue over the thenar and hypothenar eminences and even on the soles of the feet. In one case the writer observed even a slight invasion of the face. Only the back of the hands and the backs of the feet escape invariably the lipomatous invasion. In consistence the swelling is resistant, but much less so than in the nodular form. The mass is spontaneously painful and tender to pressure. Sometimes the suffering owing to the universal tenderness is very great. Occasionally it is such as to prevent movement on the part of the patient and to immobilize him in his bed.

Of the three forms the most common is the nodular. It presents a special physiognomy, which makes its recognition easy. The localized diffuse form resembles certain forms of ordinary lipomatosis, but it is, notwithstanding, differentiated by the pain and other characteristics still to be considered. The pains are never absent. They are present either spontaneously or are readily elicited by pressure. Usually they manifest themselves in both of these ways. Most often they precede the appearance of the edematous swelling. Sometimes they come on at the same time as the swelling; more rarely they are not noted until after the swelling has made its appearance. Slightly marked and intermittent, they become more violent when the disease is established. The pains are described by the patients as stinging, burning, pinching, darting, or even lancinating. Most commonly they are darting and radiate or diffuse in and about the nodules. They do not follow the large nerve trunks or indeed any nerves.

The patient describes them as though they were situated in the thickness of the masses. The muscles, the bones, and joints are not painful. The pains are exaggerated or brought on by pressure or handling. If the fatty accumulation is considerable, movement and effort may increase the pain to such an extent that the patient may be obliged to remain perfectly quiet during the paroxysm or indeed continuously. There is one characteristic which one finds in all cases, namely, the paroxysmal exacerbations already described. Suddenly and without cause or following an effort or trauma the patient again feels active pain. At the same time the new formations increase in volume; if it concerns a nodule the latter is surrounded by an edematous zone more or less extended; if it is a case of diffuse swelling the skin in this region becomes more tense and the circumference of the mass increases. As the pain subsides, the swelling recedes, but never to its former dimensions. After each crisis, the volume of the new formation is increased.

All or almost all of the patients present the symptoms of a general asthenia. The patient is very readily exhausted. Even in cases in which the muscular development is good, this fact is early noted. In cases which are advanced the asthenia is very pronounced. Sometimes this is so marked that the patient is unable to leave the bed. Sometimes she is unable to change even her position in bed largely because of her weakness, but also because of the pain and the enormous increase in the size and the weight of the limbs and body generally.

The psychic symptoms are not constant. However, they are very frequently present. A cerebral asthenia or ready cerebral exhaustion is rarely absent. Many patients present in addition great irritability; this is at times so great as to be attended by a change in character and disposition. The least opposition may enrage the patient and not infrequently she will quarrel with her neighbors in the wards to such an extent that isolation becomes imperative. Sometimes she thinks that the other patients and the nurses are against her. The sleep is usually broken and disturbed by distressing dreams and nightmares. One of Eshner's patients was disturbed mentally to such extent as to necessitate her commitment to an asylum. Hale White's case had two attacks of mental disturbance. Giudiceandrea has noted delusions of persecution and a true dementia.

In several cases lessened sensibility to touch, pain, and temperature have been noted. In the writer's first case there were found areas of anesthesia, while in other areas the sensibility was diminished. The same patient complained of velvety sensations in the finger tips and in the soles of the feet. The case reported by Henry presented marked disturbances of sensation. Touch, pain, and temperature were sometimes not perceived; at other times confused. In Giudiceandrea's case the sensibility to pain, on the other hand, was much increased, especially in the regions corresponding to the adiposed masses. The thermal sensibility, again, was particularly exquisite in the regions in which there was no trace of the neoplasms. Hyperalgesia was noted by Achard and Laubry. Patients have also complained of sudden sensations of cold or heat, of formication, or of cramps in various parts of the body. Headache is not rare.

Disturbances of the special senses are quite frequent. In some observations there was noted a narrowing of the visual fields; in others various subjective sensations, such as phosphenes, muscæ volitantes; in one case amaurosis was noted, which began to disappear from the day that thyroid treatment was instituted, and in a case of the writer there was present a circinate retinitis,—a mass of partly fibrinous and hemorrhagic exudate in the center of the retina, surrounded by crescents of fatty degeneration in Mueller's fibers.

Diminution of auditory perception has been noted several times. In some cases tinnitus more or less marked has been recorded. Smell and taste were impaired in one of the writer's cases.

Vasomotor disturbances have been very frequently noted. The skin over a nodule may present no changes whatever; on the other hand, it may be noted to be somewhat injected during a crisis of pain, or much veined and slightly bluish. Occasionally the face is much flushed,—the malar regions, the frontal regions—or it may be the neck, although no actual induration or swelling accompanies the change in color.

In some cases cyanosis of the extremities and transitory edema have been noted. Frequently also the patient notices that his flesh bruises very readily, and it is not uncommon to note small ecchymoses on various portions of the limbs and trunk, and at times these evidently make their appearance spontaneously and independently of trauma. Perhaps, in keeping with this fact is the history, not infrequently obtained, of excessive menstruation or even of metror-

rhagia. At times also epistaxis and, in one of the writer's cases, even hematemesis are noted.

Trophic changes in the form of ulcerations, blebs, and bullæ have been observed.

It is important also to add that there is quite commonly a marked dryness of the skin. Patients themselves comment upon this and examination confirms it.

Adiposis dolorosa with involvement of the joints. (*Dercum.*)

Among unusual complications noted in adiposis dolorosa are changes in the joints. Attention was first directed to this by Renon and Heitz, who in 1901 presented a case of "adiposis dolorosa with multiple arthropathies," before the Neurological Society of Paris. In addition to the usual symptoms of the affection there were present marked pain, creaking, and limitation of movement in numerous joints. A skiagraph of the left knee failed to reveal any alteration of the articular surface. The knee-cap, however, was a little thickened, and its structure offered a somewhat mottled appearance. The synovial membranes gave rise to a slightly opaque shadow, which was especially evident at the *cul-de-sac* under the

quadriceps tendon. This shadow, In-froit, who made the skiagraph, re-garded as due to fatty thickening of the synovial membrane.

In 1902 the writer placed on record (Philadelphia Medical Journal, Decem-ber 20th) a second case of adi-posis dolorosa with involvement of the joints. Skiagraphs revealed no changes whatever in the bones, but some thickening of the tissues about the joints, especially about the knee-joints. The conclusion was justified that there was present a marked thickening of the synovial membranes and possibly of other structures in the neighborhood of the joints. There was a marked tendency to the forma-tion of fringes and rice bodies. The joints appeared, as the patient ex-pressed it, to be "loose," and motion was attended by considerable pain. That the changes observed were due, in part at least, to fatty infiltration, and that this fat was painful, just as was the fat in the tumor masses on the surface of the body, afforded the most reasonable explanation of the condition. It was possible also that an actual synovitis was present. Rheumatism could not offer an ade-quate explanation of the conditions found, while rheumatoid arthritis was excluded by the absence of changes in the bones and cartilages. More recently Price has made studies in the joints of two other cases con-firming these findings.

A most interesting case of adiposis dolorosa in which bony changes were noted in the dorsal vertebræ and in the ribs has been placed on record by Price and Hudson (Journal Nervous and Mental Diseases, April 19, 1909). Kyphoses with corresponding de-formity and reduction in size of the vertebræ were noted in the dorsal region and confirmed by the skia-graph. Similar changes were noted in the ribs. The authors call atten-tion to the possible significance of these findings when the frequency of pituitary changes in adiposis dolorosa is borne in mind.

The course of adiposis dolorosa is essentially chronic. Its progress is slow, the patient being worse or better by turns in accordance with occurrence of paroxysms of pain. In well-established cases the suffering is continuous, subject always to more or less marked exacerbations.

In the majority of cases the patients become extremely obese, the weight often running from 200 to 300 pounds; in others again, in the nodular form, the weight may undergo only a moderate if any increase.

The symptoms may be briefly sum-marized as follows: fatty deposit, pain, general asthenia, and psychic symptoms. The deposits are present either in the nodular, a localized dif-fused or a generalized diffused form. The distinction between these forms is of course not absolute, as combina-tions of the various forms—or transi-tional states—may be found in one and the same patient. The deposits are found most commonly over the trunk, shoulders, arms, and thighs; the forearms and legs being less fre-quently affected and the hands and face almost never. Pain and tender-ness upon manipulation of the swell-ings are present; spontaneous pain, pain occurring in paroxysms, is also present unless it happens that the patient is observed during an interval between paroxysms. Involve-ment of the nerve trunks is rare, though it has been a few times observed, not-

ably in a case of Bergerson's. Anesthesias are rare, hypesthesias not uncommon, paresthesias are frequent; the latter consist, as already pointed out, of sensations of numbness, cold, burning, tingling, crawling.

The general asthenia and the mental phenomena have been already sufficiently considered.

The tendon reflexes may be normal or increased, but are usually diminished and sometimes abolished. In one case, that of Delecq, the skin reflexes were lost. Coincident gross nervous disease has been noted several times. Hemiplegia and aphasia were noted in one case; in another, a case of the writer, a sclerosis of the columns of Goll was revealed at the autopsy, and in still another there was involvement of the lateral tracts.

ETIOLOGY. — It is occasionally noted that the patient presents a neuropathic heredity; not infrequently grave nervous disorders are noted among the ancestors or collateral relatives. Now and then it is noted that other members of the family are unusually stout, *e.g.*, in 1 of Eshner's cases the mother was obese. In a few instances adiposis dolorosa has been observed in members of the same family. Thus, Cheevers reported the case of a man whose father and sister both had the disease, while Hammond reported 2 cases occurring among sisters. The striking fact in the etiology is the predominance of the female sex; the ratio is about 6 women to 1 man. The age at which the disease makes its appearance is exceedingly variable. The youngest recorded case, that of Hale White, began at 12 years of age; the oldest case recorded was 78 years of age. According to Frankenheimer, the majority of cases in men occur between 30 and 40 years of age, and in women between 30 and 50 years.

The disease was originally believed to occur exclusively in women and about the climacteric period; although this was the rule in the writer's experience, he has known it to begin as early as 12, and has seen 3 cases in males. He describes in detail 5 cases of the affection, 4 in women whose ages range from 20 to 42, and 1 in a man aged 47. These cases all presented the characteristic symptoms of the disease. The panniculus adiposus was invariably thickened, sometimes to a marked extent. The skin was red and in dependent parts has a bluish, livid appearance. It was painful, sometimes with a feeling of burning, at other times as if it were being pierced by a needle. The skin of the legs especially, but occasionally that of the trunk and arms also, was thick and infiltrated, generally in patches, but in some cases in large areas involving the whole lower extremity except the feet. The latter condition is described by the writer as "elephantiasic edema." Actual edema was not present, the skin did not pit on pressure, and no fluid was obtained on puncturing with a needle. Charcot observed this condition in connection with individuals suffering from functional disturbances of the nervous system, and named it "œdème hystérique." Strubing (Archiv f. Dermat. u. Syphil., Feb., 1902).

Case of adiposis dolorosa, or Dercum's disease, believed to be unique, in a newborn infant. The writer was called in consultation to see the child on the day after its birth. It was then 5 weeks old, and, in addition to the characteristic irregular symmetrical deposits of fat, which were situated on the upper half of the body (the lower extremities being normal), there were two cystic formations of considerable size, one on the left posterior aspect of the neck and the other on the left breast. While lying undisturbed the child appeared to be entirely comfortable, but the slightest movement was attended with pain. W. C. Walser

(Boston Med. and Surg. Jour., June 30, 1910).

Occasionally the patient presents a history of antecedent alcoholism or of syphilis. As Price says, the toxic effects of alcoholism and syphilis are well known and the fact that they frequently cause degenerative changes in the ductless glands has been emphasized by Lorand. This is suggestive when we learn of the rôle which the ductless glands appear to play in adiposis dolorosa. In a case described by E. W. Taylor, the disease developed while the patient was convalescing from an acute alcoholic neuritis. In quite a number of cases excessive menstrual flow and even uterine hemorrhages have been noted. In one case, that of Spiller, the adiposis dolorosa followed pregnancy, while in another, that of Schlesinger, it followed an abortion. Quite a number of cases finally have developed after the menopause.

Occasionally trauma is noted in the history, and the importance of this fact has been especially insisted upon by Guidiccandrea. In a case of the writer's and in one of Eshner's, trauma seemed to be the direct exciting cause. Emotional shock has also preceded the onset, as in the case of Achard and Laubry. In Vitaut's case there appeared to be a mild infection of the digestive tract; in other cases exposure to cold and dampness, rheumatism, appeared to play a rôle. Occasionally also some other neurosis exists side by side with the affection, as in the woman reported by Henry and in a man reported by the writer, both of whom suffered from epilepsy. In other cases again, undoubted mental disease has been noted; sometimes indeed, as in one of Eshner's cases, commitment to an institution becomes necessary.

Case of adiposis dolorosa in a woman aged 80, the mother of 5 children, who had fallen 15 years before, after which accident an operation was performed upon her hip, some bloody fluid being evacuated. Since that time her legs have been weak. Pain appeared in the left hip and lumbar region, always along the nerves. She grew stouter very gradually. The fat is in large masses about the malleoli, hips, calves, buttocks, abdomen, forearms, and backs of the arms especially. Debove (Presse méd., July 17, 1901).

Case in a woman, aged 61 years, who, with an apparently unimportant family history, dates her troubles from a fall from a chair years before. The left eye became blind, and the left side of the nose developed a tumor. The adiposis appeared in her thirtieth year, in the right leg first, and then in the left. The arms were next attacked. Pain accompanied all the early symptoms. When examined, the patient's neck and the subclavicular region, as well as the abdomen, besides the limbs, were loaded with fat. An enormous fatty tumor was also present on the internal aspect of the left thigh. The buttocks were immense. The pores of the skin were enlarged. Pain, lasting two or three days, in the fatty region was not uncommon. Sensation and temperature were normal; the corneal reflex was absent, as well as the patellar and Achilles. Mentality was normal, but there was great asthenia. The writers attribute the disease to some affection of the pituitary. Delucq and Alaux (Presse méd., Sept. 17, 1904).

A typical case with the onset of the disease at the early age of 14, and the symptoms also unusual. Generally the deposits of fat are tender, and spontaneous pains (commonly of a neuralgic or rheumatic order) are slight and only appear occasionally; in this case, however, there was scarcely any pain on pressure, and there were spontaneous burning sensations and an inner sensation of great tension. The writer attributes

these intermittent pains to a probable accumulation of water in the fatty tissue, and perhaps in the musculature also. Gräfe (Münch. med. Woch., Mar. 19, 1920).

PATHOLOGY.—Up to the time of writing, eight autopsies have been held. These indicate that in adiposis dolorosa there is some disturbance of the internal secretions, excessive formation of fatty tissue, and an interstitial neuritis of the nerve-fibers contained in the deposits.

[Price has summarized the results of the various autopsies as follows:—

CASES I and II.—Dercum: Macroscopic disease of the thyroid, the glands being enlarged and the seat of calcareous infiltration.

CASE III.—Dercum: Irregular atrophy of the thyroid, extensive interstitial neuritis of peripheral nerves in fatty deposits, degeneration in the columns of Goll.

CASE IV.—Burr: Glioma of the pituitary body; colloid degeneration, with atrophy and absence of secreting cells in many acini of the thyroid gland; interstitial neuritis of terminal filaments; sclerotic ovaries.

CASE V.—Dercum and McCarthy: Adenocarcinoma of pituitary body, thyroid normal, right suprarenal gland hypertrophied, hemolymph-glands, interstitial neuritis, undeveloped testicles.

CASE VI.—Guillain and Alquier: Hypophysis doubled in size, with marked increase of connective tissue in the glandular portion and changes suggesting an alveolar carcinoma; thyroid hypertrophied, with increase in connective-tissue stroma.

CASE VII.—Price: Inflammatory changes in thyroid, with marked increase in the interstitial connective tissue, one whole lobe being especially infiltrated, the other showing compensatory hypertrophy. Inflammatory changes in hypophysis, with presence of a condition suggesting alveolar or glandular carcinoma, interstitial and parenchymatous neuritis, sclerotic ovaries.

CASE VIII.—Price: Marked increase in the connective tissue of the thyroid gland, dilatation of the acini, with infoldings of the cuboidal epithelial lining. The same changes in the hypophysis as were found in Cases VI and VII, but less marked. No abnormalities of the adipose tissue. F. X. DERCUM.]

Delecq thinks that disease of the thyroid, testicle, ovary, and pituitary body may be causes of adiposis dolorosa. Von Schroeter concludes that adiposis dolorosa is due to a dysthyroidismus. Pineles regards the disease as a result of the disturbance of function in numerous blood-glands and that there are present hypothyroidism, genital atrophy, and changes in the hypophysis.

The thyroid gland, it will be noted, showed unmistakable changes in 7 of the 8 autopsies. These changes are very interesting and are well illustrated by the findings in the third autopsy of the writer, in which the gland was submitted to microscopic examination. A study of the sections reveals the gland to be made up of three or four different kinds of secreting tissue. In the first place, there are large acini distended by colloid material. These large acini vary in size, and their contents vary also in density. The larger acini are globular in shape, while some of the smaller ones are elongated or angular in form. The limits of these acini are clearly indicated by blood-vessels which occupy their walls. The epithelium is a single layer, which covers uniformly the peripheries of the acini. Contrasted with these there is another kind of secreting tissue, which is very solid, and in which the acini are made out with great difficulty. They consist of cells filling interspaces of the stroma, and the blood-vessels supplying these acini can only be made out in exceptional instances. The lumina of these acini when they can be made out are usually very small. There is here a

complete absence of colloid material. In other portions acini are observed which are a transition between the more solid nests of cells and the large vesicles which contain the colloid material. In addition, there is a third form of acinus, which is of peculiar interest in that the acini present plications or papillary outgrowths of the walls. These plications or outgrowths project into the lumina of the affected acini, which contain, as a rule, colloid material of lighter staining qualities than the larger vesicles, although not lighter than is contained in some of the smaller vesicles. The epithelium of these last-mentioned acini appears at times to be slightly higher than the normal cubical epithelium of the other vesicles. Finally, in some areas, solid masses of cells resembling lymphoid cells are seen, but these are probably young solid acini, like the small acini described above, though the limits of these acini are irregular, because of the absence of preserved blood in the surrounding vessels and of the absence of definite interstitial framework.

The changes observed are indicative in part of hypertrophy. Certainly this seems to be the only interpretation which can be placed on the numerous small acini which appear to be in process of development. Whether the large acini, distended with more deeply staining colloid material, are to be considered old acini, containing old or altered colloid material, it is, of course, impossible to say, but such an interpretation does not seem improbable. The plications and papillary outgrowths observed in some of the acini are also worthy of comment, in that they evidently represent an attempt to increase the secreting surface of the acini and are again expressive of hypertrophy.

These findings are very surprising, and it is difficult, of course, to frame an explanation. It is not impossible that we have here a hypertrophy which is the direct outcome of a general atrophy of the gland; in other words, a compensatory hypertrophy such as Halstead obtained in the dog after partial extirpation. The gland was small, perhaps sufficiently so to determine compensatory hypertrophy. It is probable, however, that other factors, c.g., qualitative changes of function, also played a rôle in the peculiar symptoms from which this patient suffered. It is not inconceivable that as a result of deranged thyroid action some substance was thrown into the circulation, which at one and the same time prevented the proper oxidation of the hydrocarbons of the food and tissues, and also acted as a cause of neuritis and nerve degeneration. Whatever the explanation, it is interesting to recall the diminished sweating and the occasional slowness of speech and mental irritability. The interpretation is somewhat difficult; the obesity and the dryness of skin suggest thyroid deficiency, while the flushing of the face, the occasional tachycardia, and the psychic symptoms would point rather to thyroid excess, and it is safer perhaps with Pineles to regard the condition as one of dysthyroidismus.

Among the most significant findings, however, are the changes noted in the pituitary body. In 5 of the 6 cases in which the pituitary was examined, it was found diseased. Thus Burr described a glioma of the pituitary, Dercum and McCarthy adenocarcinoma, Guillain and Alquier changes suggest-

ing an alveolar carcinoma and Price changes likewise suggesting alveolar or glandular carcinoma in 2 cases. The detailed findings in the case of Dercum and McCarthy are very interesting.

The pituitary body was closely adherent to the dural lining of the sella turcica, and an attempt at removal of the gland revealed a calcareous layer from 1 to 3 mm. in thickness, between the dura and the gland substance. When this was removed, what appeared to be the normal portion of the gland occupied the left quarter of the mass; the remaining three-fourths consisted of a tumor mass. It was of the same consistence as the gland structure, roughened on the surface where the calcareous plate had been removed, and attached at its farthest end to the internal carotid artery.

The calcareous plate under the microscope showed a true bone reticulum infiltrated with the eosinophilic cells comprising the tumor mass. Sections were made transversely through the gland and tumor. The tumor mass was composed almost entirely of the eosinophilic type of cells, arranged irregularly, with a minimal amount of interstitial tissue. Around the periphery of the tumor mass the cells were arranged in parallel rows, much after the type of cell arrangement seen in endotheliomata. The tumor mass had, on account of the arrangement of the cells in rows at its periphery, an appearance as if it were encapsulated and separated from the normal gland tissue. A careful study of the cells of the tumor revealed no trace of a regular arrangement of the cells, such as is seen in the acini of the normal gland. The individual cells were round, stained a pinkish red with eosin, and contained a small, deeply staining nucleus. The

nucleus in some of the larger cells was very large and irregular in shape, such as is frequently seen in proliferating cells. The cells varied greatly in size: some were twice the size of the normal gland cells; others one-third to one-fourth that size. Between these cells, and at times in the capillary vessels of the tumor mass, small areas of colloid material were seen.

The area of normal gland tissue— i.e., arranged according to the normal gland structure—is about one-third the size of the normal adult gland, and is situated between the tumor mass and the protuberance, consisting of cerebral tissue. The larger portion of the glandular acini is perfectly normal. At the junction of the latter with the nerve tissue, and extending into the latter area, are large groups of cells, following an alveolar arrangement and differing from the rest of the section by the deep staining properties of the cells with nuclear stains. The posterior portion of the gland, composed of reticular nerve tissue, is permeated by the small, round, deeply staining nuclei in such a way as to give the impression that the infiltrating process followed definite lymph-channels. At the periphery of the acinous portion of the gland, masses of colloid material, of sufficient size to be visible to the naked eye as minute dots, are inclosed in areas lined by rounded cells. The tumor mass, composed as it is of the same type of cells as make up the acinous portion of the gland, must necessarily belong to the carcinomata. The infiltrating tumor formation, beginning in the acinous portion of the gland and involving the cerebral portion of the gland, follows the cell arrangement of an adenocarcinoma. The arrangement of the eosinophile cells of the tumor mass

around the periphery of the tumor resembles an endothelioma, but the type of cell points strongly to a diagnosis of carcinoma.

In commenting upon the involvement of the pituitary in the above instance, the writers pointed out, that bearing in mind the interrelation which exists between the thyroid gland and the pituitary body, the pituitary body is thus brought into relation, though perhaps indirectly, with a fat-producing or fat-destroying function—a relation which, up to that time, had not been considered. In the light of recent observations this subject assumes a new importance. Froelich has shown that, instead of the symptom-complex termed acromegaly, lesions of the hypophysis may be associated with an adipositas universalis and genital atrophy. In other words, hypopituitarism, other things equal, leads to adipositas. Further curious and remarkable interrelations of function—seemingly antithetical—appear to exist between the pituitary and the pineal gland,—the pineal gland appearing to have a fat-producing and a fat-destroying function inversely to the pituitary. For a detailed presentation of the subject, which here would lead us too far afield, the reader is referred to Otto Marburg's interesting paper on "Adipositas Cerebralis, a Contribution to our Knowledge of the Pathology of the Pineal Gland," Deutsche Zeitschrift für Nervenheilkunde, 1908, Bd. 36, p. 114.

In his discussion of the pathology of adiposis dolorosa, Price points out that sufficient attention has not been given the pituitary, which, he suggests, is etiologically of almost as much importance as the thyroid. It would appear, indeed, from the above considerations that the pituitary must be seriously

considered, and he asks the question whether the symptom of adiposis dolorosa may not result from primary disease of either the pituitary or the thyroid gland. It is well known that a close interrelation exists between these two glands; experimental extirpation of the thyroid in animals has been found to be followed by pituitary enlargement and it would seem that disease of one gland means sooner or later disease of the other. Poirier also directs especial attention to the hypophysis, which he evidently regards as the most important structure concerned in adiposis dolorosa.

An examination of the fatty deposits reveals not only the structure of fatty tissue, but also the signs of great nutritional activity. Fragments removed during life by the Duchenne trocar in the writer's first case and submitted to microscopical examination presented the appearance of a connective tissue embryonal in type. The cells were voluminous, fusiform and containing large nuclei, while the intercellular spaces were filled by a transparent substance apparently without structure. On the whole the appearance was that of a lymphoid tissue. In some fragments fat cells were numerous and among these were cells which evidently had not undergone complete fatty transformation. In some of them the nuclei were still very apparent, while osmic acid revealed fat drops suspended in the cell contents.

In the autopsy recorded by Dercum and McCarthy, the fatty nodules were submitted to microscopical examination with the following result. Each of the larger nodules was composed of capsules inclosing large numbers of small, oval, fatty bodies connected with each other and with the capsule by delicate

fibrous bands. These delicate trabeculæ united and joined thick, jelly-like bands attached to the capsule. Sections made through the connective-tissue capsule and the fatty bodies *in situ* gave the following structure: The capsule was composed of several layers of well-developed connective tissue. Within this capsule a looser areolar tissue is met. This tissue is highly vascular, and between the vessels is a reticular tissue, denser in some areas than others and inclosing a large number of mono-, nuclear cells, a few polynuclear cells, and large numbers of cells staining a tawny color by the Van Gieson stain. Scattered through the granular, tawny masses many of the mononuclear type of cells may be found. In other areas granules of blood-pigment in clumps may be seen. Wherever the connective-tissue trabeculæ penetrate into the congested fat nodule, this same fine, reticular structure, holding in its meshes rich plexuses of blood-vessels, and between these a fine reticulum of connective tissue filled with a light-yellow granular material, with nucleated yellow cells, small mononuclear cells, polynuclear reagents, as do nucleated red blood-cells, and numbers of degenerating red blood-cells, may be seen. Some of these cells react to many of the staining corpuscles, but to the Biondi-Ehrlich triple stain they appear more as mononuclear leucocytes. This tissue is identical in structure with the hemolymph-glands found in the immediate neighborhood of the large, congested nodules of subcutaneous fat.

Lying loose in the yellow fat, several small, firm bodies, the size of a split pea and of a yellowish-brown color, were found. These proved on microscopic examination to be hemolymph-glands. They were composed of a cap-

sule of connective tissue, from which trabeculæ of connective tissue spread in many different directions throughout the body. Within this trabecular network a rich plexus of capillaries was found. Between the capillaries a fine meshwork of fibers contains large numbers of lymphoid cells, with here and there groups of red blood-corpuscles. Free blood-pigment giving the iron reaction was found in small quantities free in the trabecular network. The
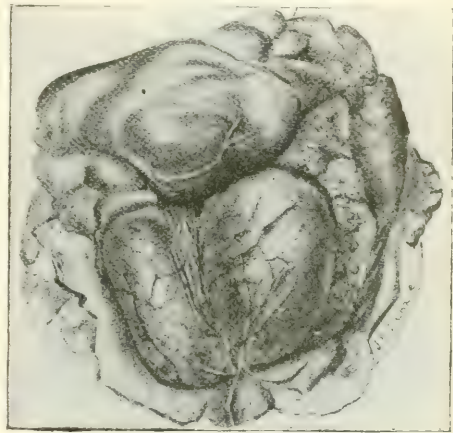
Fatty nodule dissected from subcutaneous fat: shows the encapsulation of the fat, with nerve-fibers branching over it. (*Dercum and McCarthy.*)

opinion of Dr. Simon Flexner that these structures are new-formed hemo-lymph-glands was confirmed by that of Dr. A. S. Warthin, of Ann Arbor, who has written on the subject.

An examination of the nerves found in the fat has shown the presence of an interstitial neuritis. There is a diminution of nerve-fibers, together with a marked proliferation of the perineurium and endoneurium. (See illustration, next page.)

The chemistry of the subcutaneous fat was investigated by Edsall, who especially sought for an increase in the fatty acids as this might have had to do with the pain and tenderness.

However, marked free acidity was not present. Its amount was rather low, lowest of all in the tumor fat, and decidedly below that of normal fat. The significance of this fact is not evident.

Case in which there concurred adiposis dolorosa with well-marked myxedematous manifestations. In view of the frequency of myxedematous symp-

Section of nerve in subcutaneous fat nodule showing interstitial neuritis. A distinct overgrowth of connective tissue is present between the nerve-fibers. The number of blood-vessels is also increased over normal nerve-tissue. (*Dercum and McCarthy.*)

toms in adiposis dolorosa, we are justified in accepting a kindred cause of both syndromes. That thyroid insufficiency stands at the foundation of myxedema there can be little doubt; again, some thyroid alteration was found in 4 out of 5 cases of adiposis dolorosa which came to autopsy. While the seat of the externally visible pathognomonic symptoms of myxedema is in the subcutaneous tissues, that of adiposis dolorosa is situated in the fatty structures.

Moreover, the improvement of case reported following the administration of **thyroid extract** seems to evince with certainty that perverse thyroid function was, to say the least, an antecedent. The yielding of both symptom-complexes to the same medication again points to their interrelation or their springing from a kindred cause. Thyroid therapy cannot, therefore, be utilized as a test of differentiation between myxedema and adiposis dolorosa, as some authors maintain, because both syndromes may vanish under its influence, and, as in the present instance, even at the same time. Heinrich Stern (Amer. Jour. Med. Sci., March, 1910).

Case of adiposis dolorosa in young soldier. The symmetrical and extremely painful subcutaneous lipomas were accompanied by profound asthenia, with the picture of typical Dercum's disease. The first lipoma developed about 1 month after an exceptionally violent effort to lift a heavy stone, during which the shoulder had become dislocated. The pain was intense and the previously robust young man grew weaker as more lipomas developed. They lay free in the subcutaneous adipose tissue and were easily removed. The writer concludes that the cause is some upset in the balance of fat production, the result of multiple disturbance in the endocrine-sympathetic systems. C. Martelli (Tumori, May 18, 1918).

The identity of Dercum's disease as a disorder of the sympathetic system was pointed out by Sajous in 1914, in a paper read before the Southeastern Branch of the Philadelphia County Medical Society, and also in abstract in the 1917 Supplement Volume of the Seventh Edition of the present work, page 65. EDITORS.

DIAGNOSIS.—The diagnosis is based upon the presence of the fatty masses, presenting the feature of pain, spontaneous, paroxysmal, or elicited by manipulation, and having in addition the physical peculiarities

already described. The disease is readily differentiated from myxedema because of non-involvement of the face and hands and because of the absence of pain in myxedema. When the tumor masses are numerous and small, they might suggest neurofibromatosis, but the peculiar character of the swellings, the fact that they appear lobulated under palpation, that they are spontaneously painful and almost never occur upon the face or hands would serve to make the differentiation.

In neurofibromatosis, again, there are two kinds of tumors, some of them cutaneous, not rarely on the face, and others on the mucous surfaces. They are of soft, yielding consistence and very slightly painful. Others, those of nervous origin, are small, very hard, and often grouped along the course of the nerve trunks like a string of beads. They are only laterally mobile, while the adipose tumors are mobile in all directions and are irregularly distributed. Again, anomalies of pigmentation are rare in adiposis dolorosa, but are frequent and sometimes very pronounced in neurofibromatosis. On the whole, it is hardly probable that an error could be made.

In simple obesity, the fat is distributed throughout all the tissues and does not heap itself up in separate lipomatous masses, such as is the case in adiposis dolorosa,—even in the so-called diffuse form. Besides, ordinary obesity is painless and is a matter of gradual development, while the fatty deposit in adiposis dolorosa is painful and occurs as the result of successive crises.

PROGNOSIS.—Adiposis dolorosa is an affection which is essentially chronic. Most cases live for many years and it does not appear to immediately threaten life. However, in cases of long standing, a bed-ridden period eventually ensues; general exhaustion becomes more and more marked; degeneration and failure of the heart muscle, pulmonary congestion, or a renal complication may terminate the picture. The resistance to infection also appears to be greatly diminished, for one of the writer's cases died very rapidly of an attack of erysipelas.

Cases in a relatively early stage of development—more particularly cases with small nodular or localized and limited deposits—offer a distinctly better prognosis and are distinctly amenable to improvement. Advanced cases, cases with very extensive deposits, marked asthenia, and especially with the tendency to subcutaneous hemorrhages and hemorrhages from the mucous membranes are very unpromising.

TREATMENT.—In the treatment of adiposis dolorosa one remedy has in a few cases proved of value and that is **thyroid** substance. This should be given in doses of from 2½ to 5 grains three times daily, for a very long time. The **salicylates,** notably **aspirin,** are of decided value in relieving the pain. The best plan of procedure, as a matter of course, is to place the patient in bed, and to institute a systematic course of treatment. The **rest** should be absolute and should extend over several months of time.

Typical case with symptoms of myxedema in which the treatment consisted of an antiobesity diet, **thyroid** medication, and physical therapeutics, especially **vibratory massage** and **exercise.** Nine months later the patient presented her-

self to show the beneficial effects of the treatment. Excepting the pallor, which, she said, had always caused her much annoyance since her early youth, she looked very well. She felt strong, and was able to walk from five to eight miles a day; she experienced no shortness of breath on ordinary exercise, but perspired mildly when she walked briskly. The fat bunches had disappeared almost entirely; the neuralgic pains had ceased about four months earlier; there was no tenderness on pressure on the location of the former fat masses. The skin in the supraclavicular regions and in the face had been quite tender. She evinced not the slightest mental depression and apathy, but, on the contrary, displayed a healthy optimism. Her weight had been reduced to 161 pounds. Heinrich Stern (Amer. Jour. Med. Sci., March, 1910).

Case in a man of 32, married 6 months, which, the writer thinks, throws light on the etiology of the disease. The pressure of the man's body against his desk explained the unusual location of lipomas, and the immediate effect of an injection of pituitary extract on retention of urine confirmed the influence of the pituitary on the innervation of the bladder, but the primal factor in Dercum's disease seems to be some abnormal or lacking hormone from the organs of reproduction. This seems to upset the normal balance in the chromaffine system. His patient was clinically cured, even to the retrogression of the lipomas, by systematic treatment with **thyroid 1** part; **pituitary,** 1 part, and of **ovary** 2 parts, supplemented by a **vegetable diet** and **exercise** in the country. Whenever this treatment was interrupted, the whole set of symptoms returned, even including some of the tumors. The patient learned to make his organotherapeutic products himself, making a cold extract of thyroid and testicles, 1:4, from sheep 1 or 2 years old. (Extraction cold; 50 c.c.; phenol, 0.05.) He took a teaspoonful of this extract morning and evening in warm soup. The writer re-

calls that Dercum in describing his first case of adiposis dolorosa noted its connection with the thyroid. Cecikas (Jour. Amer. Med. Assoc., from Grece Méd., Jan. to June, 1918).

Case of typical adiposis dolorosa in a girl of 16 whose menstruation had been suppressed several months. The pains returned at monthly intervals. Great improvement was observed under **ovarian extract.** After 2 years of suspension menstruation returned, and since then the paroxysms of pain had been much less pronounced. The pituitary seemed normal in radiograph, as also the thyroid. In another case, a young officer, there were small slightly movable lipomas on the forearms, absolutely symmetrical, which had developed when he was 16. Bourdinière (Progrès Méd., Sept. 7, 1918).

The patient should be weighed when treatment is begun and thyroid substance given at first in small and then in somewhat larger doses. At the same time a **diet** should be instituted that is largely free from carbohydrates and fats. It should be remembered, however, that a diet, no matter how rigid, will of itself make no impression in adiposis dolorosa; it will fail absolutely. It is of course wise to institute a careful diet, but patients do better when the diet is not too strict. Inasmuch as the affection is attended by a marked asthenia, the diet should be nutritious. It should consist of the red meats in moderation, the white meats freely, the succulent vegetables, eggs, and skimmed milk. The latter can be used between meals and if necessary also at mealtimes.

The pains are not infrequently controlled or at least made better by **aspirin** or **salophen** in full doses, 10 or 15 grains three times daily after meals. Sometimes the tenderness

and soreness are better borne when the limb or part affected is gently supported by a flannel roller; if the tenderness be extreme a layer of cotton-wool may first be applied.

Just as soon as the tenderness permits, **gentle massage** should be instituted; sometimes this can never be employed; in other cases again it can be instituted comparatively early and there can be no doubt that in a measure it favors the diminution of the swellings, especially if the patient can bear deep kneading. **Bathing between blankets** as in ordinary rest treatment should also be carried out, but of themselves baths accomplish nothing in adiposis dolorosa; indeed the physical exertion and manipulation attendant upon the application of ordinary hydrotherapeutic measures in these cases exhausts the patient.

It is a good plan to keep a record of the pulse and temperature during the thyroid administration, although the writer has never observed any fluctuations of moment in these cases, even when the thyroid was pushed. The patient should, of course, be weighed from time to time and the dose of thyroid modified according to the impression made. In some cases no impression whatever can be made; in other cases again the impression is decided. In 3 cases of the writer, the result was most satisfactory; 2 of these were treated systematically by rest in bed; the third could not for certain reasons be put to bed. In all 3 the improvement in the size of the swellings and in the lessening of pain was very great. Treatment was carried out six months to a year. In 1 case the affection recurred at the end of two years, but was again con-trolled. In the second, improvement and practically good health has persisted for four years. The third was greatly improved and has disappeared from observation.

The experience of the writer with cases in the hospital wards and out-patient departments has been very unsatisfactory partly because many of the cases were greatly advanced, the deposits being enormous and the asthenia grave, and partly because the cases could not be kept systematically under treatment for a sufficiently long period.

General tonics, **iron, arsenic, strychnine** may be given, but they do not help appreciably. Electricity is useless. Finally, it would in the judgment of the writer be perfectly justifiable to attempt the surgical enucleation of a specially painful mass; this procedure has not yet been attempted. We should bear in mind, of course, that these patients have but a feeble resistance to shock and often present, even to superficial examination, marked cardiac weakness.

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ADIPOSITAS CEREBRALIS.
See Obesity and Acromegaly.

ADONIS VERNALIS.—Adonis is a ranunculaceous plant, closely related to the anemone, growing wild in Europe, Asia, and Africa. Several species of adonis are employed,—*Adonis vernalis, A. æstivalis, A. capensis, A. cupaniana,* and *A. amurensis,*—but all seem to possess the same properties, although the several varieties are variously employed in the different countries in which they grow. In Russia, for instance, it has long been employed in cardiac diseases, and in Africa as a

substitute for cantharides, the bruised leaves, when fresh, possessing vesicating properties.

DOSE.—An infusion of 4 to 8 parts of the plant in 200 of water may be given in tablespoonful doses three or four times a day (Huchard). The tincture may be administered in doses of ½ to 1 dram (2 to 4 c.c.). The fluidextract has also been used in doses of 1 to 2 minims (0.06 to 0.12 c.c.).

Cervello isolated a glucosid from *Adonis vernalis,*—adonidin,— a yellow, hygroscopic powder having a bitter taste, obtained from the leaves. It is soluble in water and alcohol, but insoluble in ether or chloroform. Adonidin is administered in doses varying from ⅟₁₆ to ¼ grain (0.004 to 0.017 Gm.). It acts more promptly than digitalis.

Inoko also obtained a glucosid—adonin—from the Japanese plant, *Adonis amurensis.* This substance is free from nitrogen, amorphous, colorless, of a bitter taste, and soluble in water, alcohol, and chloroform. The effects observed on the heart of a frog were precisely those seen when digitalin is used. It is about twenty times weaker than the adonidin obtained from the European *Adonis vernalis.*

PHYSIOLOGICAL ACTION.— Adonis resembles digitalis in its action upon the heart when given in therapeutic doses. It increases cardiac energy and raises the arterial tension. The increased contractions eventually diminish and a period of quiet follows, varying in duration with the dose administered.

> In frogs and dogs the watery extract caused a marked slowing of the heart, owing to stimulation of the pneumogastric and its terminal branches, the blood-vessels being contracted and the blood-pressure raised. The alcoholic extract, on the other hand, had a very slight effect on the frequency of cardiac contractions, but increased their strength and also dilated the blood-vessels, the blood-pressure remaining unaffected. Slovtzoff (Roussky Vratch, Sept. 15, 1912).

The prevailing knowledge of the mode of action of adonis is based on experiments with the glucosid adonidin. The results have, on the whole, been contradictory. While Cervello and Lesage found that it arrested the heart in systole, Huchard and Hare ascertained repeatedly that this organ was arrested in diastole and Guirlet found the left ventricle in systole and the other cavities in diastole. There has been greater concordance in respect to its effects on the blood-pressure, all observers having found that there was first a rise, then a fall.

While the primary slowing is attributed to the inhibitory action of the vagus, since its section prevented it, Hare found that the diastolic arrest was not due to this nerve, since it occurred after the latter was divided, while galvanization of the nerve later on also failed to inhibit the heart. He concludes, therefore, that adonidin tends secondarily to paralyze the vagus—Kakowski, in fact, found that it caused dilatation of the coronaries instead of contraction of these arteries. Hare's experiments indicate that it may also cause primary stimulation and secondary paralysis of the vasomotor system.

Adonis has been credited with diuretic properties by Bubnow, Altmann, and Michaelis, though their observations have failed to be con-

firmed by certain others. Whatever diuretic power it may have is probably the result of activation of the renal circulation (Wood).

An unmistakable cumulative action and a marked action on the heart was observed by the writer. The patient had taken 6 Gm. (2½ drams) of the drug in an infusion daily for 56 consecutive days—a total of 396 Gm. (13⅕ ounces). He was a large man of 65, hearty, with mitral insufficiency and alcoholic cirrhosis. There were no signs that the drug was proving toxic, no headache, nausea nor pain in the stomach, but the pulse of 43 then developed a typical bigeminus form. On suspension of the drug the beat returned to the normal type in the course of 3 days. Mayor and Segond published in 1912 a research showing that the digestive juices have a destructive action on the active principle of adonis. Roch (Arch. des Mal. de Coeur, June, 1913).

INCOMPATIBILITIES. — T h e glucosid adonidin in solution is decomposed by free acids or alkalies. It is incompatible with tannic acid, corrosive sublimate, and silver nitrate. The physiological incompatibilities of adonis include aconite, amyl nitrite, muscarin, veratrum viride.

CONTRAINDICATIONS.— Adonis is contraindicated in arteriosclerosis, in affections attended by a high vascular tension (as in the earlier stages of interstitial nephritis), and in hypertrophy and other disorders of the heart in which digitalis, its physiological homologue, is harmful.

THERAPEUTICS.— Adonis is useful in cases of **valvular heart disease** with loss of compensation and in which evidences of grave circulatory disorder, such as cardiac asthma, are present. It has been specifically recommended in **aortic** and **mitral regurgitation.** The

diuretic powers of the drug cause it to be of value in cases of **dropsy** and **cardiac degeneration.** It is also valuable in **palpitation** dependent upon irregular inhibition. As it does not seem to possess cumulative tendencies, it may be administered with more freedom than digitalis. According to Dujardin-Beaumetz, however, large doses cause gastric disorders and vomiting. Borgiotti found adonis valuable in different **cardiac disorders.** One dram to 1 ounce of the infusion daily constitutes an excellent cardiac tonic. In **fatty degeneration of the heart** it increases diuresis and regulates the circulation.

Adonidin is credited with properties superior to digitalis, in that it acts more promptly and with less tendency to cumulation. As Dujardin-Beaumetz had observed in the case of the infusion of adonis, however, Lublinski and Durand have found adonidin to produce violent gastrointestinal disorders with diarrhea and vomiting. According to Dujardin-Beaumetz, the dose should never exceed ⅓ grain (0.02 Gm.) ; Huchard gives 1/12 grain (0.005 Gm.) three or four times daily in adults.

As a remedy for the reduction of **obesity,** adonis æstivalis has proved of value. Owing to the fact that it does not possess a tendency to cumulation, it may be continued for a long time. It is claimed to have been effective in relieving the heart from an excessive covering of fatty tissue. The tincture of this species may be given in doses of 10 minims (0.6 c.c.) three times daily.

To reduce the active cerebral hyperemia present during a paroxysm of **epilepsy** adonis has been recommended, owing to its power of stimu-

lating the vasoconstrictors. It may be advantageously combined with the bromides.

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AND
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ADRENALIN.—See ANIMAL EXTRACTS: ADRENALS.

ADRENALS, DISEASES OF THE.—Although it is the purpose of this Cyclopedia to present the prevailing or current views upon the subjects treated, the writer does not feel that he can conscientiously observe this rule in the present instance. Having probably devoted more time to the study of the ductless glands and to a comparative analysis of the work done by others than any other investigator in this comprehensive field, he does not hesitate to state that the physiological rôles that physiologists now attribute to the adrenals are not true functions but merely secondary expressions of a function first described by myself in 1903. It is, briefly, that the adrenals sustain tissue oxidation and metabolism by contributing an oxidizing ferment to the hemoglobin.

What I deem to be only manifestations of that function, are: (1) Oliver and Schäfer's theory that the adrenals sustain the cardio-vascular tone; (2) Cannon and La Paz's emergency theory, in which the adrenals are thought to secrete only under the stress of excitement, fear, anger, etc., and (3) Abelous and Langlois' theory in which the adrenals are thought to carry on an antitoxic rôle, mainly for the destruction of fatigue wastes. All these theories have been severely attacked by other physiologists, Stewart, Hookins, Gley and others, and it is generally considered at present that they are obsolete. From my viewpoint, however, such is not the case, for if, as I hold, the adrenals govern respiration and tissue oxidation (a function admittedly obscure according to physiologists), it is but normal that they should sustain the vascular tone, secrete abnormally under the influence of excitement, and take part in breaking down fatigue wastes.

It has also been shown that adrenalin is able in small doses to lower the blood-pressure. This is due from my viewpoint to the fact that it primarily causes constriction of the vasa vasorum; the arterial supply of the vascular muscularis being reduced, the vessels dilate.

To understand the rôle of the adrenals in disease it is important to understand the following:—

The Adrenal Secretion in Pulmonary and Tissue Oxidation.—The prevailing diffusion doctrine as to the absorption of oxygen from the pulmonary air and the elimination of carbonic acid, having been shown by Paul Bert, Müller, Setschenow and Holmgren, Bohr and other authorities to be defective, Bohr concluded in 1891 that some internal secretion capable of taking up the oxygen from the air in the lungs was necessary to explain the process. A comprehensive study of the question led me to the conclusion that it was the internal secretion of the adrenals which carried on this all important function. The following are but a few of the main factors in support of this opinion:

1. *The marked affinity of the adrenal secretion for oxygen,* sustained by the experimental observations of Vulpian, Cybulski, Langlois, Battelli, Abel, Takamine and others, including the writer.

2. *The presence of the adrenal secretion in the venous blood between the adrenals and the pulmonary air cells,* sustained by the experimental observations of Gottschau, Manasse, Aulde, Stilling, Pfaundler, Cybulski and Scymonowicz, Biedl, Langlois, Dreyer,

Salvioli and Pizzolini and personal anatomical researches.

3. *The marked reducing power of the blood coursing in the walls* of the air-cells, shown by the experiments of Robin, Verdeil, Garnier, and Müller.

4. *The presence in the hemoglobin, of a constituent whose physicochemical properties are those of the adrenal secretion,* sustained by the observations, first, of Vulpian, Gautier, Moore, Moore and Purinton, and Cybulski as to the properties of the adrenal principle; those of Battelli, Dixon and Young as to the presence of the adrenal principle in the blood; of Mulon as to its presence in the red corpuscles; of Schmiedeberg, Jaquet, Abelous and Biarnès, and Salkowski, and my own as to the presence of an oxidizing ferment in the blood; of Jolles and Poehl as to the catalytic and oxidizing properties of the adrenal components of the blood.

5. *The adrenalin secretion can endow hemoglobin with its oxygen-carrying power* sustained by the observations of Menten and Crile (1915) that the blood of the adrenal vein invariably assumed a bright red color in from one to twenty minutes after dilution with salt solution, while blood from other organs treated in the same manner showed no change—a fact found spectroscopically to be due to an increased formation of oxyhemoglobin. Again, Menten (1917) having added adrenalin to diluted human venous blood, found that it caused an increase in the intensity of the oxyhemoglobin absorption bands.

6. *The presence of the hemoglobin containing the adrenal principle in all parts of the body, including the skin,* sustained by the presence of melanins everywhere and their identity as hemoglobin derivative and as the adrenal principle based on the investigations of Leonard Hill, Hirschfeld, Chittenden and Albro as to melanin being an hemoglobin derivative; those of Boinet, Mühlmann, and myself as to the identity of melanin (the bronze pigment of Addison's disease) as a product of the adrenals.

7. *The marked influence of the adrenal secretion and preparations upon the temperature, general oxidation, and metabolism,* sustained by the observations of Reichert, Morel, Lépine, Israel, and others, including myself, as to their ability to cause a rise of temperature; those of Brown-Séquard and many others, as to the steady decline of temperature following removal of the adrenals, or occlusion of the adrenal veins; the hypothermia of Addison's disease; the observations of Byelaventy, Ioteyko, Dessy and Grandis, and others, including myself, as to the increased gaseous interchanges and cellular metabolism, and the increase in the elimination of waste products caused by the adrenal principle.

The Adrenal Secretion in Immunity.— The adrenal secretion in this connection is, from my viewpoint, but *one* of the antibodies which carry on this process, being what has been termed by Bordet the "fixative" or "specific immunizing body" and by Ehrlich "amboceptor." Referring to "Internal Secretions" for details which cannot be embodied here, upon this phase of the question, I will limit myself to the direct relationship of the adrenals with the autoprotective functions:—

The adrenals are known to carry on antitoxic functions. Sustained by the observations of Albanese (1872), which showed that removal of the adrenals reduced the resistance to poisoning by neurine; those of Abelous and Langlois (1892-1898), which showed that the adrenals neutralized poisonous substances derived from muscular activity and bacterial products, and also by the investigations of Mosse. Additional testimony is afforded by the marked evidences of overactivity shown by the adrenals under the influence of certain waste products and toxins, as noted by Langlois and Charrin, Petit, Stilling, Auld, Wybaux, and others, and also by the protection afforded by adrenalin injections against strychnine injections observed by Oppenheim, Meltzer and Auer and various toxemias and infections as observed by Hoddick, Netter, Marran and Dare, Moizard, Kirchheimer, and many other clinicians.

The relationship between the adrenals and general oxidation, shown above, also establishes a connection with the production of *fever,* which, in the light of modern work is also considered, up to a certain limit, as a defensive process. C. E. DE M. S.]

To disregard functions of such importance would make it impossible to account for many phenomena awak-

ened by disorders of the adrenals, and correspondingly limit our usefulness in the practical field. This entails, however, the necessity of granting to the adrenals a position in pathology equal to any of the major organs. Indeed, the functions I have attributed to them, in addition to those with which they are already credited, entitle them to rank pathogenically with the heart and blood-vessels in so far as the general vascular pressure is concerned, and the lungs in respect to respiration and tissue oxidation.

When, moreover, their rôle in the autodefensive or immunizing processes of the body is also taken into account, their importance may almost be said to exceed that of other organs; since they thus not only serve to sustain life through tissue oxidation, but also to protect life through their rôle in immunity.

CLASSIFICATION.—Impairment of these functions to any extent, through factors which either inhibit or exaggerate the secretory activity of the adrenals, must necessarily awaken symptoms which indicate the functional disorders present. In Addison's disease (treated by Prof. Langlois, of Paris, earlier in the present volume), for example, where destruction of the adrenals or of their secretory nerves by a local lesion correspondingly compromises their functions, we have as main phenomena not only the vascular hypotension and cardiac weakness which the well-known action of the adrenal secretion on the blood-pressure explains, but also the low temperature, the general coldness, the dyspnea and the gradual emaciation which deficient oxidation alone accounts for. Now if, from any cause, the functions of the adrenals are inhibited, we have a reproduction, more or less marked according to the degree of inhibition, of these morbid phenomena. They form the symptom-complex of the condition best designated by the term "hypoadrenia."

[This term was selected owing to its greater exactness and brevity than "hypoadrenalism," and owing to the fact that the latter suggests the presence of a habit such as "alcoholism." It is obviously less cumbersome than "insufficiency of the adrenals" or "adrenal insufficiency," and corresponds with terms in current use such as "anemia," "asthenia," etc.

In 1899 Sergent and Bernard (Archives Générales de Médecine, July) were the first to advance the view that adrenal insufficiency was a syndrome due to destruction of the adrenals, but standing apart from Addison's disease, which they ascribed mainly to lesions of the abdominal sympathetic. My own researches ("Internal Secretions," vol. i, 1903, and ii, 1907) sustained the opinion of many other observers, however, to the effect that the elimination of Addison's disease was not warranted, and that this disease presented the most comprehensive external picture of gradual destruction of the adrenals or of the periadrenal sympathetic structures, or of these structures and the adrenals jointly, i.e., of adrenal insufficiency.

Again, Sergent and Bernard ascribe the syndrome of adrenal insufficiency as a whole to a general intoxication which they divide into fulminant (sudden death), acute (rapid autointoxication), and subacute (slow autointoxication). From my viewpoint, however, all the symptoms excepting the convulsions are due to the inhibition of functions which are primarily dependent upon the adrenals: viz., general oxygenation, metabolism, and nutrition. The only intoxication phenomena, the convulsions witnessed in these cases, I ascribe to the accumulation of toxic wastes (shown by Abelous and Langlois to be antagonized by the adrenal secretion) which are not broken down with sufficient rapidity when the oxidation processes sustained by the adrenals are inhibited. C. E. DE M. S.]

Of the various forms of hypoadrenia is one which is practically unrecognized, though frequently a cause of death, mainly among children, viz.:—

TERMINAL HYPOADRENIA.

DEFINITION.—Terminal hypoadrenia is a form of marked asthenia which occurs late in the course of an acute febrile disease as a result of exhausting secretory activity of the adrenals—acting as defensive organs—in the course of that disease.

[The term "terminal" is ˙ serted here because it is important to differentiate this form of hypoadrenia from that which occurs early in the course of a toxemia and known as adrenal hemorrhage, treated farther on in this article. C. E. DE M. S.]

PATHOGENESIS AND SYMPTOMATOLOGY.—The adrenals being admittedly concerned in the protection of the organism during infections and intoxications, by contributing an excess of their secretion during the febrile stage of the disease (sometimes considerably prolonged), it follows that, after this stage is over, the adrenals should lapse into a condition of more or less temporary insufficiency through fatigue or exhaustion. That other organs concerned in the immunizing process are influenced in the same way must doubtless be the case, but the fact remains that it is the symptomatology of hypoadrenia that is uppermost.

In lobar pneumonia and bronchopneumonia, for instance, resolution may be considerably delayed and convalescence likewise. There is, late in the case, extreme adynamia and a low blood-pressure, the temperature is below normal, the pulse weak and more or less rapid, and death from heart-failure is not infrequent. In typhoid fever, hypoadrenia is commonly observed. The disease assumes what is now known as the cardiac type, with, late in the case, extreme prostration, a rapid, weak and sometimes irregular pulse, hypothermia, and a marked tendency to vertigo, fainting, and cardiac failure.

[Sicard (Bull. de la soc. méd., July 21, 1904) reported the case of a young woman in whom the foregoing symptoms appeared on the ninth day of a bronchopneumonia. Extreme muscular weakness, marked hypothermia and low blood-pressure, diarrhea, and Sergent's white line, which denotes marked adrenal insufficiency, were present. On the fifteenth day the blood-pressure fell to 70 or 80 (7 or 8 per cent. potain) and death followed three days later. At the autopsy the adrenals were found hemorrhagic. This suggests that adrenal lesions may be present in all such cases. Yet, Ribadeau-Dumas and Bing (Bull. de la soc. anat., June 3, 1904) have witnessed the same symptoms in cases of measles which recovered, while Bossuet (Gaz. hebd. des sci. méd. de Bordeaux, Oct. 30, 1904) refers to 8 cases in various febrile disorders in which typical symptoms of adrenal insufficiency, asthenia, low blood-pressure, etc., developed suddenly and disappeared spontaneously, aided perhaps by adrenal extract which had been administered.

As stated recently by Morichau-Beauchant (Le progrès médical, Oct. 9, 1909), the adrenals seem to show a special predilection for certain infections. Diphtheria easily leads them all in this connection. So seriously do these organs suffer in these cases that Sévestre and Marfan have termed the type "secondary syndrome of malignant diphtheria." Hutinel ascribes the fulminating cases of scarlatina to this cause. Tetanus, erysipelas, mumps, certain forms of tonsillitis, and certain streptococcic infections may also present the typical syndrome of hypoadrenia. Goldzicher (Wiener klin. Woch., June 10, 1910) was led by his researches to conclude that in the various forms of septicemia the appearance of lower blood-pressure was to be ascribed to insufficiency of the adrenals. C. E. DE M. S.]

When, at the end of an infectious disease, the case, instead of proceeding to convalescence, remains in a condition of asthenia, with low blood-pressure and temperature, there is good ground for the conclusion that terminal hypoadrenia has occurred. Exhaustion of the adrenals during the acute process having inhibited the secretory activity

of these organs, the above symptoms result from inadequate oxidation of, and metabolic activity in, the tissues. Sergent's white line, brought about by gently rubbing a narrow streak over any part of the abdomen with the finger, may be obtained in the majority of these cases. After a short period the area becomes whitish and remains so a short time.

The writers found the white line present in 145 out of 228 cases; 65 of these had hypotension and 80 a normal or hypertension. The 83 cases which did not give the test included 30 with hypotension and 53 with normal or hypertension. The 80 cases with the white line without hypotension and 30 with hypotension without the white line make a total of 110, or one-half of the 228 cases tested, which do not conform to the rule. They conclude that the white line cannot, therefore, constitute a sign of either adrenal insufficiency or hypotension. Lautier and Grégoire (Soc. de biol., vol. lxvii, p. 690, 1910),

In a special research for the presence or absence of Sergent's white line in 100 sick or wounded soldiers in a garrison infirmary, the line was elicited in 81. It was present in all but 2 febrile cases and in 17 out of 20 subjects with gonorrhea. It was never absent in grip, rheumatism, malaria, or tuberculosis, and was encountered in a variety of purely local conditions, as gingivitis and orchitis. The writer concludes that the white line is of great value in certain emergencies of differential diagnosis, as when acute *adrenal insufficiency* is confused with a pyrexia of meningeal, thoracic, or abdominal origin. Its association with certain infections like grip and rheumatism means a certain degree of asthenia and hypotension, and betrays the implication of the adrenals in the disease picture, though not as serious as acute adrenal insufficiency, with collapse, and does not carry a bad prognosis. Finally, when encountered in associa-

tion with some trivial local condition, it represents a mere coincidence, or is due to a transitory disturbance of vasomotor equilibrium. Baudron (Jour. de méd. et de chir. prat., July 25, 1918).

The patient complains of chilliness; the surface is pale, owing to the poverty of the blood in cellular elements and hemoglobin, and to recession of the blood-mass from the surface to the deeper vascular trunks. The vascular tension being low, the pulse is rapid and the heart-beat weak. Anorexia, due to deficient metabolism and diminished demand for food, nausea, the result of relaxation of the gastric muscular coat, and diarrhea, due to a similar condition of the muscular coat of the already passively engorged intestine, and more or less frequent fainting spells, are all concomitant symptoms that may be witnessed in such cases, which are always greatly exposed to relapse or to sudden death from heart-failure.

The author has observed nine cases of acute suprarenal insufficiency of variable intensity, ending in recovery. The symptoms develop very rapidly, and, besides, they can disappear spontaneously, at the same time with the illness which they accompany, for this acute adrenal insufficiency is due to an infection or an intoxication. The writer has always noted that the insufficiency occurs in the course of a toxic or infectious malady, medical or surgical. G. Bossuet (Gaz. hebd, des Sci. Méd. de Bordeaux, Oct. 30, 1904).

Case of acute insufficiency of the adrenals in an apparently healthy farmer who had been doing some hard work, exposed to the sun for several hours, when suddenly he collapsed with intense abdominal pain and headache, with great prostration. On the presumptive diagnosis of sunstroke, he was treated with cold to the head and purgatives, but the symptoms persisted, soon accompanied by vomiting and hiccough; the

prostration increased, with a tendency to stupor; there were intense headache and delirium, respiration was superficial, the pupils were dilated and did not react to stimuli, the heart-sounds became faint and death occurred at the end of the week. The only pathological findings at autopsy were atrophy of the adrenals from a sclerotic process in the veins, and compression from a hematoma from rupture of one of the veins in the adipose tissue surrounding the left suprarenal capsule. The writer attributes the acute insufficiency in his case to excessive exposure to the heat of the sun. Sotti (Policlinico, Jan. xv, Med. Sec. No. 1, 1908).

Symptoms arising in the course of scarlatina which are very suggestive of insufficiency of the suprarenals. The symptoms are asthenia, depression, failure of the heart-power, hypotension of the arteries, tendency to syncope, abdominal pains, and a brown coloration of the skin. The use of small doses of adrenalin had a remarkable effect in the cases cited, the patient recovering after being in an apparently desperate condition. V. Hutinel (Le bull. méd.; Med. Record, Sept. 18, 1909).

The 2 most prominent symptoms of terminal hypoadrenia in *typhoid fever, acute nephritis, pneumonia, scarlet fever,* and *diphtheria,* noted by the writers, were a sudden fall of blood-pressure and extreme prostration but hypothermia, vomiting, a profuse green diarrhea, and an erythematous rash were also commonly observed. The adrenal lesions were found to differ, being either hemorrhagic, or granulofatty, and ending in necrosis. Dumas and Hervier (Bull. et mém. de la Société méd. des Hôp. de Paris, 1913).

The symptomatology of the terminal hypoadrenia in the various infections, *measles, diphtheria, erysipelas, scarlet fever* and others, is virtually identical in all, asthenia, low blood-pressure, prostration, hypothermia, vomiting, pain in the epigastrium, though two or more of these symp-

toms may dominate the picture. Daily doses of 12 to 20 minims of adrenalin daily in such cases, cause the disease to lose its menacing character as regards cardiac arrest. V. Hutinel (Arch. de Méd. des Enfants, March, 1915).

The writers observed 3 cases of sudden death from *pernicious malarial fever* in soldiers. In all 3 cases there was hypotension coinciding with maintenance of regular cardiac rhythm. In 1 of the cases the suprarenal white line pointed out by Sergent was clearly identified. In all 3 cases there were found lesions of the adrenal cortex. Paisseau and Lemaire (Acad. de Méd., Oct. 17, 1916; Monde Méd., Jan., 1917).

The adrenals are frequently involved in camp diseases, including *dysentery, malaria* and *gas gangrene,* and the writer reports a case of *anthrax septicemia* in which cardiovascular disturbances were pronounced from the first. The young man suffered from intense pain in the epigastrium, with profuse vomiting and final hematemesis, evidently due to elimination of the microbes or their toxins by the gastro-intestinal mucosa. The extremely low blood-pressure and imperceptible pulse were explained by the necropsy findings of edema of the anterior mediastinum, compressing the pericardium, and destruction of the left suprarenal by a recent hemorrhage. Roger (Paris méd., July 14, 1917).

Complications of various kinds may occur. The immunizing processes being greatly weakened through the deficiency of adrenal secretion, one of its important factors, septic infection, abscesses, bone lesions, tuberculosis of a rapid type, and other infections may more or less rapidly develop. Disorders of nutrition, cholelithiasis, and occasionally Addison's disease may also appear. In acute pulmonary infections, pneumonia, for example, organs in the neighborhood of the focus of infection,

the pleura, the mediastinal glands, etc., being inadequately protected by the blood or its phagocytic cells, become the prey of specific bacteria. Briefly, the body is rendered vulnerable to the attacks of almost any pathogenic organism.

PATHOLOGY.—In the special type in question no adrenal lesion may be discernible. In the majority of instances, however, the organs are enlarged and congested and may show, here and there, a limited hemorrhagic area. Their appearance suggests not only the functional torpor incident upon functional exhaustion, but the presence of a *passive* congestion resulting from loss of resiliency of their sinusoidal vessels, thus impeding the circulation through them. Occasionally they are the seat of suppuration, a complication which is apt to be observed when the causative disease is, or includes, a streptococcic infection, pneumonia, or meningitis.

The pathological picture of the more severe form of adrenal complications, *i.e.,* intercurrent *hyperadrenia,* shows far more distinct lesions of the adrenal parenchyma. Hence the typical lethal phenomena that attend many of these cases.

> Mott and Halliburton have found already that in cases of death from exhausting diseases the adrenalin present in the adrenals was diminished or absent. The writers have extended these observations; they have examined the adrenals in the cases of 50 adults dying from various diseases. The glands were placed in Cohn's fluid for twenty-four hours and afterward stained with Scharlach or Sudan III; by this method the chromaffinic substance and the fat were demonstrated. They relied upon this demonstration of the amount of chromaffinic granules in the cells of the medulla, and did not

carry out the physiological test. No appreciable loss of the substance occurred during twenty-four hours following death, as told by control experiments in animals. Adrenalin was always being given off, especially if the splanchnics were stimulated. The conclusions drawn from their work were that in cases of acute infection and rapid death adrenalin was absent in the medulla; this applied also to cases of death from shock and from peritonitis when, in short, the blood-pressure was low. On the contrary, in chronic diseases, such as phthisis, adrenalin was to be found in the medulla. In cases of high blood-pressure adrenalin was present and distinctly increased. F. A. Bainbridge and P. R. Parkinson (Brit. Med. Jour., Mar. 11, 1907).

In 25 experiments on guinea-pigs and hedgehogs, the writer found that in only three was the microscopic condition of the adrenals approximately normal, while in the remaining 22 very characteristic changes were present, which in 18 were of serious degree, consisting of hemorrhages and necroses, alone or combined, after poisoning with the diphtheria toxin. Strubell (Berl. klin. Woch., March 21, 1910).

The influence of *diphtheria* toxins upon the secretory activity of the adrenals is well shown by personal experiments in which poisoning of an animal with diphtheria toxin was found to cause, at first, an increased proportion of adrenalin in the blood and subsequently a gradual decrease until total disappearance of the adrenal principle had occurred. Tscheboksaroff (Berl. klin. Woch., June, 1911).

The writer convinced him that these organs are invariably the seat of lesions, and that the gravity of the latter depends more upon the intensity of the attack than upon its duration or associated infections. Moltschanow (Rev. del Circ. Med. Argentino, Nov.-Dec., 1912).

The writers found that *acute peritonitis* showed a very marked reduction of adrenalin, and that in 50 per

cent. of the cases of this disease examined *post mortem*, the adrenal cortex showed marked histological lesions. The authors conclude that acute peritonitis takes the lead among infections in the production of adrenal lesions, a fact which explains the circulatory failure so marked in this disease. Reich and Beresnogowski (Beitr. zur klin. Chirurgie, May, 1914).

TREATMENT.—In these particular cases the use of **adrenal gland,** or of **pituitary body,** which acts very similarly but with less violence and more lasting effects, sometimes gives surprising results. The adrenal product—which, from my viewpoint, is also the main active agent in the neural lobe of the pituitary, as shown by the chromaffin test—supplies precisely what the body needs, *e.g.,* the resumption of all oxidation processes (thus restoring general metabolism and nutrition), and a rise of blood-pressure, which causes the blood to circulate normally in all organs, including the skin and the adrenals themselves. Indirect effects are also obtained: its action on the heart increases the contractile power of this organ, which is thus rendered capable of projecting the blood with more vigor through the lungs, and causes oxygenation of the blood to become more perfect. Recovery is also materially aided by the rise of blood-pressure that the adrenal product insures, causing, as it does, arterial blood to be driven from the splanchnic area toward the peripheral organs, including the lungs and the brain. From these features alone considerable benefit is derived.

If we recall, moreover, the participation of the adrenal secretion (which the adrenal preparation administered represents) in the immunizing process, we have the added factors of ridding the blood of any intermediate—and therefore toxic—wastes, bacterial toxins, etc., it may contain, and of increasing phagocytic activity, thus antagonizing efficiently any pathogenic organism that may remain to compromise the issue.

Thus explained, we can understand the phrase, "little short of marvelous," applied to the results obtained by some clinicians. We can also understand the marked reduction in the mortality obtained by Hoddick (Zentralbl. f. Chir., Oct. 12, 1907) in cases of peritonitis following appendicitis accompanied by uncontrollable decline of the blood-pressure, cyanosis, and other evidences of collapse, and also in puerperal toxemias, by the slow intravenous use of adrenalin in saline solution. Hoddick ascribes the lowering of the blood-pressure to paralysis of the vasomotor center; but as the toxemia is the cause of this condition, an agent capable of counteracting both cause and effect is necessary. This is met by the adrenal principle. Josué (Soc. Med. des Hôpitaux, May 21, 1909), in typhoid fever, likewise relieved threatening symptoms by injecting 15 minims (1 c.c.) of **adrenalin** (1 : 1000 sol.) in ½ to 1 pint (250 to 500 c.c.) of physiological **saline solution** subcutaneously. The influence of the saline solution in these cases must not be overlooked, however. Eight years ago I urged that death was often due, in infectious and septic diseases, to the fact that the osmotic properties of the blood became deficient, and advised the use of saline solution *from the onset* of the disease. The reduction in the mortality of pneumonia in the practice of men who have carried out this suggestion has demonstrated its value.

[Several clinicians have employed much larger doses of the adrenal active principle with profit. Marran and Darré (Jour. des praticiens, May 15, 1909) found it of great value in the collapse of diphtheria

with marked asthenia, low blood-pressure, and subnormal temperature. Moizard (Revue de thérap., Jan. 1, 1910) recommends adrenal organotherapy as soon as asthenia and low blood-pressure occur in any infection. He gives daily two sheep's fresh adrenals, finely divided and mixed with powdered sugar, or administers the active principle, 10 to 20 drops daily divided in five or six doses. Kirchheimer (Münch. med. Woch., Dec. 20, 1910) has found large doses, 10 to 24 minims, safe hypodermically in the collapse of pneumonia, diphtheria, and scarlet fever. Letulle has found it of great value in the latter disease. The better plan, from my viewpoint, is to inject it with saline solution (at 108° F.), intravenously, the needle of the syringe containing the adrenalin being inserted into the rubber tube of the saline solution apparatus.   C. E. DE M. S.]

If adrenal insufficiency arises during the progress of diphtheria, the writer advises combining **suprarenal opotherapy** with **serotherapy**. If syphilis is also present, suprarenal opotherapy may be associated with mercurial treatment. In the other infectious diseases, where no specific medication exists, opotherapy should be begun from the beginning of the symptoms of suprarenal insufficiency. **Adrenalin** may be given by the mouth, or, if the hypodermic method is used, 1 c.c. of a 1:1000 solution is added to 50 grams of normal **salt solution** and injected into the subcutaneous tissue. As this medication is inoffensive, it can be continued daily until the accidents of suprarenal insufficiency have disappeared. Comby (Archives de méd. des enfants, Jan., 1911).

To ascertain the most efficient dosage of adrenalin to counteract cardiovascular failure in *pneumonia, typhoid* and *paratyphoid fever,* the writer compared the effects of various doses in 30 patients. She found that 0.5 c.c. (8 minims) of **adrenalin** caused a moderate rise of blood-pressure which could be sustained by repeating the dose hypodermically every hour or hour and a half. This dose was found to be the most efficient for infectious diseases. Mansvetova (Roussky Vratch, July 4, 1914).

The writer calls attention to the morbid effects of the hardships of the European War as causes of hypoadrenia, through traumatic *shock, major injuries, typhoid fever, typhus, cholereiform diarrhea, Asiatic cholera, chloroform* anesthesia, *exhaustion,* etc. Such cases are not met by 10 to 15 drops of **adrenalin** 1:1000 solution. He gives $\frac{1}{30}$ to $\frac{1}{20}$ grain (2 to 3 milligrams) divided into 4 to 6 doses hypodermically, and in addition $\frac{1}{60}$ to $\frac{1}{30}$ grain (1 to 2 milligrams) orally. He is convinced of having successfully combated collapse with such doses which otherwise would have ended fatally. Sergent (Bulletin de l'Acad. de Méd., Sept. 7, 1915).

In the hypoadrenia of *pneumonia, diphtheria,* and *typhoid fever,* the writer found a combination of *pituitrin* and *adrenalin,* 0.25 c.c. (4 minims) of the former, and 0.5 c.c. (8 minims) of the latter, intravenously in young children and twice these doses in older children restored failing circulation more actively than all other agents. This confirmed the results of Kepinow, who had previously urged this combination. Rohmer (Münch. med. Woch., June 16, 1914).

The essential symptomatic triad of adrenal insufficiency in asthenia, is low blood-pressure, and Sergent's white line. In some cases adrenal insufficiency constitutes the entire clinical picture and seems primary; yet often close examination reveals a causative infection, at times very slight, *e.g.,* a mild throat inflammation or intestinal infection. Other forms comprise the *adrenal overstrain of soldiers;* the adrenal insufficiency of infections, such as *typhoid, diphtheria,* and *tuberculosis;* that due to *alimentary or other forms of intoxication;* that of *cardiac dilatation.* The solar syndrome (skin discoloration and lumbar pains), the latter due to involvement of the pericapsular nerve ganglia, may also be present. In such cases, **extracts of the total gland** sometimes prove distinctly superior to the pure adrenalin

otherwise used. Both these products, repeatedly given, exert a regenerating action on the adrenals. Their hypodermic and oral administration is free from the danger of causing arterial atheroma. **Adrenalin** by mouth gives good results provided it is used in sufficient amounts—1 to 4 and even 5 c.c. (16 minims to 1 or 1¼ drams) of the 1:1000 solution a day, divided into two intervals. Three c.c. (48 minims) may be thus given daily for a month or more without harm. For hypodermic use the dose is 0.5 to 2 c.c. (8 to 32 minims) a day, 0.5 c.c. being preferably not exceeded as the single dose. Such injections are generally more or less painful. Slow absorption of adrenalin is secured by injecting under the skin 250 to 500 c.c. (½ to 1 pint) of normal saline solution to which 1 c.c. (16 minims) of adrenalin solution has just been added. The skin is usually blanched at the point of injection and the adrenalin is only with extreme slowness absorbed through the contracted vessels. The pain attending this procedure is prevented by adding 0.01 Gm. (⅙ grain) of **novocaine** to the solution. The injections may be continued for several days. **Extracts of the whole adrenal** may be given orally in daily amounts of 0.2 to 0.4 Gm. (3 to 6 grains), divided into 0.1- to 0.2- Gm. (1½ to 3 grains) doses, or hypodermically in a daily amount of 0.1 Gm. (1½ grains). Josué (Paris méd., Jan. 6, 1917).

Adrenal insufficiency is a rather frequent complication of amebic dysentery, manifested in marked general depression, asthenia, a feeble pulse, etc. In the case of a soldier on the Franco-Belgian front, stationed where Senegalese and Moroccan troops had recently been, the onset of diarrhea was accompanied by prostration and tachycardia. Careful examination revealed no organic disturbance save in the liver, which was slightly tender and distinctly enlarged. The number of stools rose as high as 45 in 24 hours. The white line phenomenon was elicited on the abdomen and the pulse remained thready at 120 a minute. The diastolic blood-pressure descended to 70 mm. Hg. (Pachon instrument). **Emetine hydrochloride** in divided doses, to the total amount of 0.06 up to 0.1 Gm. (1 to 1½ grains) per diem, together with **adrenaline** and **camphorated oil**, within a few days placed the patient on the road to recovery. The use of adrenaline is especially recommended where there are signs, even slight, of impairment of the adrenals due to toxic action of the amebæ on these organs. R. Dujarric de la Rivière and Villerval (Paris med., Apr. 21, 1917).

Case in which there was unusually marked pigmentation, disappearance of the pigmentation followed suprarenal treatment. The loss of muscular strength, due to suprarenal deficiency, was very marked. Osborne (Amer. Jour. Med. Sci., Aug., 1918).

These measures are only indicated in emergency cases, however. In the average case the **glandulæ suprarenales siccæ** of the United States Pharmacopeia, administered by the mouth, is fully as effective if a good preparation is obtained as soon as asthenia and low blood-pressure appear. The powder in 3-grain (0.2 Gm.) doses, three times daily, in capsules, gradually increased until 5 grains are given at each dose, usually suffices. When the cardiac adynamia disappears, a small dose of **thyroid,** the desiccated gland, ½ grain (0.03 Gm.); **strychnine,** 1/60 grain (0.001 Gm.), and **Blaud's pill,** 1 grain (0.06 Gm.), added to each capsule, greatly hasten convalescence. The iron and the adrenal product serve jointly to build up the hemoglobin molecule, a slow process when left to itself.

For our knowledge of the action of the use of pituitary extracts in infectious diseases we are mainly indebted to L. Rénon and Delille (1907); who began their use in 1907. In a recent work in

which the clinical observations of both observers are recorded, Delille ("L'Hypophyse et la médication hypophysaire," 1909), referring to grave cases of typhoid fever, states that they showed "arterial hypotension, irregularity of the pulse (especially the grave forms), oliguria, insomnia; while convalescents showed asthenia, hypotension, or at least 'effort hypotension' (Oddo and M. Achard), paroxysmal or continuous tachycardia"—all, we have seen, symptoms of hypoadrenia or adrenal insufficiency. They found 1½ grains of **pituitary extract** (of both lobes) at noon daily extremely efficient; it counteracted at once the depressed arterial tension, produced diuresis, counteracted insomnia, and greatly improved the general condition. Similar effects were observed in diphtheria and erysipelas. The results in pneumonia do not appear to me to warrant the use of any adrenal or pituitary preparations early in the case, the first few days of the disease, when the blood-pressure and the fever are high. They should be used *only when a low blood-pressure and other symptoms of hypoadrenia are present.* The results reported by Delille strengthen this opinion. In advanced tuberculosis no beneficial effect was obtained from this treatment.

ACUTE HYPERADRENIA AND ADRENAL HEMORRHAGE.—

This condition, which may lead to fatal hypoadrenia by arresting the functions of the adrenals, is generally known under the term of "adrenal hemorrhage." The association with hyperadrenia, *i.e.,* excessive functional activity of the adrenals, introduced here, is important in that it calls attention to the cause of the lethal hemorrhage, viz., *abnormally high temperature and blood-pressure.*

[Just as *hypo*adrenia appears to me to replace advantageously "hypoadrenalism" and "adrenal insufficiency," so does *"hyper*adrenia" seem to convey more exactly excessive adrenal activity than "hyperadrenalism," which suggests habitual overactivity, besides being less cumbersome than the phase "excessive secretory activity" and others in general use. C. E. DE M. S.]

This disorder is, briefly, the result of undue activity of the adrenals. Hyperemia of these organs occurs normally, *i.e.,* physiologically (owing to their participation in the autodefensive functions of the body), in the course of all febrile infections or intoxications. When these toxemias are severe this adrenal congestion is increased in proportion—sufficiently so in some instances to cause rupture of the adrenal vascular elements, and hemorrhage within the organs. An additional cause of congestion in the latter is the abnormal rise of blood-pressure which the unusual production of adrenal secretion entails; all the vessels of the body being unduly contracted, the adrenal capillaries, which are deprived of muscular elements, are overladen with blood and prone, therefore, to rupture. These few facts are necessary to elucidate the definition of the disorder.

DEFINITION.—Acute hyperadrenia is that condition of the adrenals characterized by intense congestion of their vessels, which occurs in the course of severe febrile infections and certain intoxications, and manifested by a high blood-pressure, and in infections, also, by a high temperature. When this congestion exceeds the resistance of the adrenal vessels adrenal hemorrhage occurs, causing death when both adrenals are hemorrhagic, in a large proportion of cases, especially infancy and childhood.

[The limitation "certain intoxications" is introduced, because active congestion of the

adrenals is produced only by poisons which cause a marked rise of the blood-pressure, strychnine and quinine, for example. As shown in "Internal Secretions" (vol. i, pages 19 to 55, 4th edition, 1911), the use of such remedies in the course of infections and intoxications may do harm by increasing the congestion of the adrenals and therefore the chances of hemorrhage. C. E. DE M. S.]

SYMPTOMATOLOGY AND PATHOGENESIS.—This disorder is relatively common in children, especially in infants; death occurs, from adrenal hemorrhage, without premonitory symptoms, except, perhaps, a hemorrhagic rash or purpura—denoting excessive vascular tension—over the body, and a high temperature. The toxemia here has promptly destroyed the adrenals. As a rule, however, more or less marked phenomena, beside those due to the disease from which the child may be suffering, and varying considerably with each case, initiate this acute phase of the process, the adrenals being on the border-line of hemorrhage. These may include vomiting and diarrhea, melena, very acute abdominal pain, hematemesis, icterus, fever, with hyperpyrexia sometimes immediately before the adrenal rupture. When the hemorrhage occurs there is more or less sudden collapse, a very feeble and rapid pulse, shallow respiration and, perhaps, some bronchial rhonchi, the face being more or less dusky, cyanosed, or even livid, and the temperature subnormal. These phenomena are typical of adrenal insufficiency or failure, the adrenal secretion sustaining, we have seen, general oxygenation and metabolism and cardiovascular contractility.

Symptomatology of adrenal hemorrhage as observed in 80 cases: (1) In 46 out of 79 cases there were no appreciable signs. (2) In 5 cases there was a voluminous hematoma or abdominal tumor that could be perceived by palpation. The diagnosis was made in 1 case only during life. (3) There were peritoneal symptoms in 6 cases, all accompanied by tearing of the capsule with hemorrhage. (4) There were symptoms of capsular insufficiency in 8 cases. (5) In 15 cases there was sudden death, or death after three days at the most, sometimes accompanied by delirium, convulsions, contractures, coma, hypothermia, and syncope. In more than half of the cases, therefore, the hemorrhages remain latent and apparently without effect upon the organism. F. Arnaud (Archives gén. de méd., May, 1900).

Series of four cases of hemorrhage into the skin and suprarenal capsules, the interesting features of which were the sudden onset, rapid course and fatal termination. Not one of the patients was over a year old. The history throws absolutely no light on the causation of the disease; neither does the question of food appear to bear any relation to it. The presence of hemorrhage in the skin and suprarenal capsules would seem to make it more probable that the disease is some form of toxemia. In two cases the blood from the unopened heart was examined bacteriologically with negative results. In its extremely rapid and fatal termination the disease somewhat resembled the epidemic diarrhea and vomiting of infants. The general condition of the patients was different. They did not present the sunken eyes and the inelastic skin which is frequently met with in the epidemic diarrhea, and the cyanosis present in these cases is very rarely, if ever, seen in the skin and suprarenal capsules; the fact that Peyer's patches were much swollen is interesting. The authors believe that these symptoms are the manifestations of a special disease, and that the cause of this disease is a blood poisoning of some form, at present unknown. P. S. Blaker and B. E. G. Bailey (Brit. Med. Jour., July 13, 1901).

Three cases of sudden death in infants, due to hemorrhage into the

suprarenal capsules. The train of symptoms is very definite. A child, previously well, is suddenly seized with acute abdominal pain and vomiting, the temperature rises, and one of the exanthemata is suspected. No characteristic rash appears, however, though sometimes there is purpura. Convulsions supervene, the patient becomes moribund, and death occurs in a few hours. If the condition is an infection presumably, it is a special infection of unknown origin. Bacteriological examination has proved negative in almost every case. Langmead (Lancet, May 28, 1904).

The microscopic report was as follows: The right suprarenal showed no abnormal appearances. The left suprarenal was much broken up, but there were the remains of hemorrhage in its medullary substance, both in the form of extravasated corpuscles and as granules of pigment. B. G. Morrison (Lancet, June 6, 1908).

Case of a man 35 years old who succumbed in five days to adrenal hemorrhage. The disturbance was sudden in its onset, with symptoms resembling those of intestinal obstruction: violent abdominal pains, which morphine was powerless to relieve, continued vomiting, and absolute retention of gas and feces. Laparotomy was performed and showed the intestinal tract, including the appendix, to be entirely normal. The pain was in no way modified by operation. The temperature rose to 39° C. (102.2° F.), the pulse became extremely feeble, the respiration slow and shallow, and death took place on the fourth day after operation. The autopsy showed bilateral lesions of the adrenals, without other dangers of any kind. The left adrenal gave evidence of a recent and of a former hemorrhage (the patient had experienced a similar, though less severe, attack a few years before).

The condition of the abdomen, slowing of the pulse, with temperature remaining normal, should draw the attention from the intestinal tract to the adrenals. The case also indicates that this syndrome may not be fatal, and,

if not fatal, may recur. Brodnitz (Münch. med. Woch., July 26, 1910).

In newly born infants suffering from *erysipelas* and other infections, the writers observed a syndrome consisting of vomiting, a green diarrhea with retraction of the abdomen, an erythematous rash, and profound asthenia, leading to algid collapse. The only lesion found at autopsy in such cases was an hemorrhagic distention of the adrenals. Lesne and François (Paris Médical, June 29, 1912).

Case of an apparently well boy complaining only of slight fatigue, who suddenly became comatose, the pulse reaching 140 and the temperature 104° F. (40° C.) and died in 36 hours. The autopsy showed *initial typhoid lesions* in the intestines and a caseous *tuberculosis of both adrenals*. Méry and Heuyer (Paris Méd., May 30, 1914).

In 1 of 2 cases described, the first, occurring in a man 41 years, showed as most prominent symptoms a subnormal temperature, and slow respiration and pulse. Death followed 3 days after a nephrectomy for a pyonephrosis. Post-mortem examination showed a number of sharply defined focal necroses scattered throughout the cortical zone of the right adrenal, with degeneration of cells, polynuclear infiltration, and moderate hemorrhage of the gland. Many of the capsular vessels were thrombosed, so that this thrombosis of the vessels may be a possible cause of the adrenal lesions. E. Moschcowitz (Proceed. N. Y. Pathol. Soc., Oct.-Dec., 1917).

Case suggestive of cerebral hemorrhage. The limbs were rigid, the reflexes gone, and the pupils distinctly dilated. The face and hands were cyanosed. The temperature was 99° F. (37.2° C.). Urine was normal. Cerebrospinal fluid showed no change and gave a negative Wassermann reaction. The patient died 2½ hours after admission. The clinical course was thus apoplectiform in type. The necropsy was performed within 2

hours of death. The only organs exhibiting any marked pathologic change were the suprarenals. These were almost entirely destroyed, and converted into structureless, amorphous, yellowish masses, firm in texture, and considerably larger than the original glands. W. Boyd (Jour. Labor. and Clin. Med., Dec., 1918).

In adults, most frequently subjects between 20 and 30 years of age, the attack may also be sudden, or preceded by a period of great lassitude or asthenia. In most instances, however, the symptoms are such as to suggest acute intoxication or infection, with very severe pain, either in the epigastrium, the abdomen or below the costal margin, as the pre-eminent symptom. Then follow, in rapid succession, incoercible vomiting and, perhaps, diarrhea, and the signs of adrenal hemorrhage: great weakness of the pulse and rapid decline of the blood-pressure, hypothermia, cold sweats, coldness of the extremities, coma and death. This, may, however, be preceded by a typhoid-like state, delirium, convulsions and various perversions of the cutaneous pigmentation, varying from yellow to light-brown. In a series of 79 cases collected by Arnaud (1900) death occurred within a period ranging from a few hours to three days. The hemorrhage may be due to the rupture of a hemorrhagic cyst of the adrenals (treated under the next heading) and be preceded, therefore, by the symptoms peculiar to this condition.

The types of acute insufficiency of the suprarenals are classed by the writer as follows: (1) those of sudden onset; (2) the asthenic type; (3) the nervous type; (4) sudden death where nothing but a destructive lesion is found; and (5) cases which occur in hemorrhagic diseases. These types often overlap each other. In the asthenic type there is only extreme asthenia, followed in a few days by death. The nervous type includes those showing *convulsions, coma, delirium,* or *typhoid* states. In instances of convulsions the convulsion might well be the cause of the adrenal lesion. The first type is of particular interest because of its striking similarity to acute pancreatitis. The onset is sudden, "with *epigastric pain and tenderness,* vomiting, extreme prostration, feebleness and rapidity of pulse, coldness of extremities, lumbar tenderness, and, at times, diarrhea and abdominal distention, followed within a few days by death." The shock is more profound, the lumbar tenderness more acute, and the epigastric pain and vomiting less pronounced in adrenalitis than is usually the case in acute hemorrhagic pancreatitis.

Attention should be paid to the relative frequency of the condition in the purpuras of childhood and during or shortly after the acute infections; and due consideration must be paid to the apparent insufficiency and inflammations in the neighborhood of the suprarenals, surface burns, chronic heart or pulmonary disease, and any phenomenon tending to a great increase in internal blood-pressure. Lavenson (Archives of Intern. Med., Aug. 15, 1908).

In "Internal Secretions" (1903-1907) I called attention to the fact that many drugs influenced the functions of the adrenals, some depressing them, others overexciting them. When from any cause, these organs are debilitated the loss of their influence in the defensive functions of the body causes it to be more easily affected both by drugs, toxins, and other poisons.

Animals with adrenal insufficiency are more sensitive to intoxication of **curare** and **strychnine** than normal animals. A large number of poisons are more active in decapsulated animals than in normal ones. Camus and Porak (Soc. de Biol., June 21, 1913).

Sudden death in a man of 47 after 20 c.c. (5 drams) of a 2 per cent.

solution of **alypin** had been injected into the bladder. The only lesion found was an extensive *tuberculous process* in the right adrenal. The writer cites 3 cases from literature in which death followed at once after local anesthesia with **cocaine** or **novo-caine** and in both cases the necropsy revealed a tumor in the adrenal medulla. Proskauer (Therap. der Gegenwart, Dec., 1913).

Hypoadrenic subjects tolerate **sal-varsan** badly. When this potent agent is to be used the signs of hypo-adrenia should be looked for. If these are present the patient should be confined to bed for a couple of days after the injection of salvarsan, and adrenalin be administered sys-tematically during that time. Ser-gent (Bulletin de la Soc. des Hôp., Feb. 26, 1914).

Toxic doses of all **arsenicals** of which we have any knowledge pro-duce definite pathological changes in the adrenals of guinea-pigs. These changes include congestion, hemor-rhage, disturbances in the lipoid con-tent, cellular degeneration and necro-ses, and reduction in the chromaffin content. The character and severity of the injury produced by different arsenicals vary with the chemical con-stitution of the compounds. From these facts they conclude that ad-renal injury is an important factor in arsenical intoxication. W. H. Brown and Louise Pearce (Jour. of Exper. Med., Nov. 1, 1915).

The writer in a comprehensive clinical description of hemorrhage of the adrenals in the young as observed by him, states that the attack begins with extreme severity, high fever, vomiting, severe abdominal pain, cyanosis and often purpura, the pa-tients dying in from 6 to 24 hours after the onset of the symptoms. Friedrichsen (Jahrbuch f. Kinderh., vol. lxxxvii, p. 109, 1918).

ETIOLOGY.—That we are deal-ing with a relatively common morbid process is shown by the fact that Mattei, Rolleston and Le Conte, in 230 autop-sies in the newborn, found adrenal hem-orrhage in over 100 instances, or 45 per cent., while the proportion in adults is about 1 per cent. To explain the marked predilection of infants to this disorder many theories have been advanced: Weakness of the intra-adrenal vessels, either congenital or due to general dis-orders, such as syphilis, scorbutus, or, again, to lesions of the vascular walls, such as fatty degeneration, aneurism, etc.; lack of firmness of the medullary portion of the organ, the usual seat of the hemorrhage; compression by the uterus during labor of the inferior vena cava, thus offering resistance to the blood-streams from the adrenals which enter this great venous channel; ligation or prolapse of the funis, and other me-chanical factors capable of causing pass-ive congestion of all organs, including the friable and extremely vascular ad-renals.

While all these agencies probably cause hemorrhage in a certain propor-tion of cases, the majority are due, as stated above, to some form of intoxica-tion, either toxins or endotoxins of in-fectious origin, or autogenous poisons, such as toxic waste products or auto-toxins of intestinal origin. Some ob-servers have ascribed the morbid pro-cess to a single hypothetical organism, but it has been clearly shown that dif-ferent germs could produce it, including the *Staphylococcus aureus* and *albus* (Riesman), the pneumococcus (Hamill and Dudgeon), the pneumobacillus of Friedländer (Litzenberg and White), and others.

in adults hemorrhage occurs also, as a rule, as a complication of various dis-eases, some of which, such as septicemia, erysipelas and tuberculosis, are clearly of bacterial origin. Epilepsy, on the other hand, illustrates the class of cases

in which adrenal hemorrhage may be caused by autogenous poisons. In the adult, as shown under the next heading, several of these morbid processes may give rise to hemorrhagic cysts, which may eventually rupture into the abdominal cavity.

[That a general toxemia is an active factor in adrenal hemorrhage has been demonstrated experimentally. Roger (Le bull. méd., Jan. 21, 1894) found that inoculation of the guinea-pig by a pure culture of the pneumobacillus of Friedländer is followed by abundant hemorrhage of the suprarenal capsules, the blood bursting through the great capsular vein and causing necrosis of the elements by mechanical compression. These hemorrhages do not occur in the rabbit. Langlois (Le bull. méd., Feb. 7, 1894) saw hemorrhages produced by the pyocyaneus bacillus. Pilliet (Le bull. méd., Feb. 7, 1894) has also observed such hemorrhage after intoxication by essence and nitrate of uranium. C. E. DE M. S.]

The adrenals are exceedingly vascular, and at times are subject to emporary passive engorgement. Another cause of hemorrhage is unquestionably bacterial invasion, and several hemorrhages of considerable size have been reported as due to this cause. The hemorrhage may be also due to toxemia from irritating chemical poisons. In animals who have been injected for experimental purposes, with sera or antitoxins, as, for example, that of diphtheria, severe congestions and, occasionally, hemorrhages have occurred. A. J. M'Cosh (Annals of Surg., June, 1907).

Instance in an epileptic who died during an attack of enteritis, and in whom the autopsy revealed recent extensive hemorrhage in both adrenals. This seems to be a rare cause of death in adults, though not so uncommon in children. The reported case is one of Arnaud's asthenic type, probably due to circulatory failure from sudden removal of the tonus, producing secretion of the suprarenals. J. F. Munson (Jour. Amer. Med. Assoc., July 6, 1907).

Case of adrenal hemorrhage and acute edema of the lungs in the course of convalescence from acute nephritis due to erysipelas. The patient, a woman of 35 years, died suddenly on the fourth day of the nephritis, which had been brought on by exposure to cold. The autopsy showed, besides the evidences of pulmonary edema and intense acute nephritis, great distention of the adrenals by hemorrhage into them, with complete destruction of the medullary substance. Loederich (Le bull. méd., July 8, 1908).

From an extensive experience in autopsy work in the newly born, the writer believes that hemorrhage into the suprarenals is very common, and that the evidence is sometimes microscopic instead of macroscopic. He has found some degree of hemorrhage in infections due to the streptococcus, staphylococcus, pneumococcus. Bacillus pyocyaneus, the colon bacillus and a micrococcus he was unable to classify. We may have infections with the pneumococcus without any evidence of pneumonia. S. M. Hamill (Jour. Amer. Med. Assoc., Dec. 5, 1908).

Hyperplasia of the adrenal is an almost constant lesion in arteriosclerosis associated with chronic interstitial nephritis and left-sided hypertrophy, and it occurs with almost equal frequency in arteriosclerosis with chronic nephritis of the parenchymatous type; it is also a frequent lesion of arteriosclerosis without nephritis and of nephritis without arteriosclerosis. Adrenal hyperplasia is, consequently, probably the result of some factor active in a period of life in which these affections are most frequent. The adrenal lesion consists of increase of connective tissue, round-cell infiltration, increase in the thickness of the vascular wall and hyperplasia of the adrenal cells proper. Pearce (Jour. of Exper. Med., Nov., 1908).

PATHOLOGY.—An important function of the adrenals is to destroy products of metabolism. This was first

shown by Abelous and Langlois, whose views have been confirmed by many observers. Subsequently this function was found to apply to bacterial toxins. The prevailing view as to the pathogenesis of adrenal apoplexy is that, as a result of the *active* congestion of the adrenals incident upon infection and excessive functional activity and the high blood-pressure resulting therefrom, or *passive* congestion due to factors which prevent the free passage of blood out of the organs, such as pressure upon the adrenal veins, the inferior vena cava, etc., the capillaries become engorged and yield, thus causing a more or less diffuse interstitial hemorrhage. In some instances the entire adrenal parenchyma is destroyed, and the organ is more or less dilated by the blood accumulated in it, and may thus form a brownish or reddish-blue mass, varying in size from that of a small walnut to that of the underlying kidney. In other cases the organ ruptures, the blood flowing into the peritoneum or the abdominal cavity. Both adrenals are involved in the morbid process in most instances. Other organs, the lungs, the pleura, and skin in particular, may also be the seat of hemorrhage, the purpura witnessed in a large proportion of cases being naught else than a punctiform hemorrhage into the cutaneous tissues, due to excessive vascular tension. Death may be due to these hemorrhages or to the annihilation of the functions of the adrenals.

Small ecchymoses into the adrenals occur frequently in the various infectious diseases and are to be considered toxic in origin. Hemorrhagic infarction of both adrenals often leads to peritonitis and collapse and may result in death. It may, however, occur without any of these sequences. Large hematomata may be found in the adrenals. Hemorrhage into these glands may also occur under the following circumstances: traumatic influences (under this class is found the form seen in the newborn); hemorrhagic diathesis; thrombosis of the suprarenal veins, which is the most common cause; and bacterial capillary embolism, which occupies the second rank. The thrombi can affect the trunk or the tributaries of the suprarenal veins; they can occur in both or only in the right organ; they are to be regarded as marantic thrombi, occurring, as a rule, only in individuals suffering from some form of chronic disease. The peculiar anatomical disposition of the vessels favors their formation. A primary suprarenal disease does not precede these cases. Under the cases of bacterial capillary emboli are included those in which neither clinically nor anatomically can septic disease be observed. Bleeding into the adrenals may lead to atrophy of the organ. M. Simmonds (Virchow's Archiv, Nov. 3, 1902; Med. News, Dec. 27, 1902).

Acute hyperadrenia and adrenal hemorrhage in the infant may also be due to toxemia. While the fetus is *in utero* its waste products are transferred to the maternal blood and converted therein into eliminable products. When its birth occurs it is left to its own resources, and if it is unable fully to break down its waste products these accumulate in its blood. Its waste products—and this applies as well to certain toxins, including those enumerated above—excite powerfully both the adrenal system and the vasomotor center (hence the flushing following a copious meal). If the adrenal system can thus be made to prevail, the wastes (or toxins) will be gradually destroyed, and the vasomotor center will not be abnormally excited. If it is not, the wastes accumulate, and the vasomotor center being powerfully stimulated, the vascular tension and the blood-pressure become intense; this being further enhanced by the excess of adrenal

secretion produced, the pressure becomes such that the adrenal tissues, already overburdened with blood as a feature of their overactivity, yield — along with many cutaneous capillaries, as witnessed by the hemorrhagic purpura.

Examination of the adrenals in 16 cases of diphtheria, 10 of variola, 23 of lobar- and broncho- pneumonia, 5 of typhoid fever, 1 of tetanus and 4 of streptococcus infection. The glandular cells were profoundly altered. There was also hemorrhagic extravasation into the stroma, in which the polynuclear neutrophilic leucocytes are especially abundant. True abscess formation occurs chiefly in the prolonged infections of variola and typhoid fever. No peculiar alterations were observed as the result of special infections and the changes in general were common to all the cases examined. A pericapsular sclerosis, cortical and central, was present in most cases. This chronic lesion is not due to the acute process, but is to be regarded as the result of previous repeated or continued infections. The writers regard the adrenals as possessing an important function in the resistance of the organism to infection. Oppenheim and Loeper (Archives de méd. exper., Sept., 1901).

Case of a male infant, four days old, who was born after a normal labor. On the fourth day after birth the infant ceased to pass urine and after total suppression for twenty-four hours it died. At the autopsy the chief interest centered in the suprarenal bodies; the left one was replaced by a tumor the size of a hen's egg and the right one presented a tumor as large as a cherry at its apex. The structure of both tumors was identical, both showing a hypoplasia of the fascicular zone followed by marked fatty changes and necrosis. In the case of the growth in the left suprarenal body, liquefaction of the necrosed central portions gave rise to a cyst which was filled with cell *débris*. Both growths were considered to belong to the group of adenoma. A. S. Warthin (Archives of Pediatrics, Nov., 1901).

Results obtained by inoculating rabbits and guinea-pigs with cultures of various micro-organisms. The micro-organisms used were diplococci, typhoid bacilli, bacterium coli, *Staphylococcus aureus*, streptococci, anthrax bacilli, and diphtheritic bacilli. In the experiments with active cultures there was always great hyperemia of the suprarenal bodies and in the more active cases there were hemorrhages. E. Frederici (Lo Sperimentale, lviii, Fasc. 3, 1904).

Common pathological changes found in the suprarenals are hemorrhage, which converts the medulla of the organ into a pulpy mass, and embolism of the suprarenal artery, whereby the entire organ is destroyed. Occasionally, one or both organs will be converted into the large bluish tumors, whose contents are fluid blood. This is especially common in the newly born, and many believe that the motions necessary for artificial respiration are the real cause. In a number of cases observed by the author, however, artificial respiration was not resorted to, and it is likely that severe labor, particularly if the child is in the breech position, will furnish the necessary trauma to rupture the friable suprarenal tissue and thus give rise to a hematoma. If both organs are affected the symptoms are those of Addison's disease, and death rapidly sets in. S. Oberndorfer (Wiener klin. therap. Woch., June 18, 1905).

Conclusions based on a study of 119 cases including 2 personal cases: 1. Hemorrhage of the suprarenal capsules is more common than hemorrhage in the other viscera. 2. This is due primarily to the close relation of the adrenals to the vena cava, making congestion easy, and to the peculiar anatomical construction which favors hemorrhage. 3. A weakness of the vessel walls, either normal delicacy or pathological alteration favors

the rupture. 4. The place of election of the hemorrhage is usually in the internal cortical zone because of its vascularity and the anatomical arrangement of the vessel. 5. The bleeding always follows active or passive congestion. 6. Passive congestion may be caused by difficult labors, obstetric operations, thrombosis, or, in short, anything that would favor venous stasis. 7. Active congestion is induced by infection or any toxemia which incites hyperemia by a superactivity of the gland. 8. The findings of the pneumobacillus of Friedländer in the 2 cases personally reported and other bacteria in 5 additional cases prove beyond question that infection is a cause of adrenal hemorrhage. 9. Death results either from loss of blood or an interference with the physiological function of the gland. J. C. Litzenberg and S. Marx White (Jour. Amer. Med. Assoc., Dec. 5, 1908).

TREATMENT.—The literature of the subject is suggestively silent on the prevention and treatment of this condition. The foregoing conception of its pathogenesis, however, opens a greater field in this connection.

As to prophylaxis, it must be borne in mind that acute hyperadrenia is present when the blood-pressure and the febrile process are abnormally high. Antipyretics are worse than useless, since they further increase the blood-pressure and through this fact the danger of adrenal congestion, which may lead to hemorrhages. The physiological **saline solution** offers, on the other hand, all desirable qualities. It does not, as argued theoretically by some authors, increase the vascular tension, even if injected intravenously, as shown by the experiments of Sollmann (Archiv f. exper. Path. u. Pharm., Bd. xlvi, S. i, 1901), Briggs (Johns Hopkins Hosp. Bull., Feb., 1903), and others, any excess of fluid leaves the vessels at once. By re-

ducing the viscidity of the blood, saline solution tends to relax the blood-vessels; by increasing its osmotic properties it facilitates greatly the penetration of the plasma into the lymphatic channels, thus further reducing the vascular tension. The bactericidal and antitoxic properties of the blood are not reduced in the least by this procedure; there is considerable evidence available to show, in fact, that they are enhanced (see "Internal Secretions," 4th ed., vol. ii, p. 1367, 1911). Saline solution, therefore, should be used intravenously in emergency cases; subcutaneously in threatening cases, and per rectum in all cases in which there is any likelihood whatever that adrenal hemorrhage might occur. If employed from the *onset* of all infections, as I suggested in 1903, the blood-pressure would probably never be raised sufficiently to endanger the adrenals.

As to drugs, we have several at our disposal which lower the blood-pressure. In emergency cases **nitrite of amyl** by inhalation, with **nitroglycerin** (or, in children, the **sweet spirit of niter**) to sustain the effect, appears indicated. **Chloral hydrate** has been used advantageously by J. C. Wilson in certain exanthemata, to subdue the cutaneous discomfort and as a sedative; as it is also a vasomotor depressor, it might also serve advantageously in all but infants in whom the respiratory mechanism is defective. **Veratrum viride** suggests itself as another useful agent of this class. Of all measures, however, the saline solution is much to be preferred.

When the hemorrhage has occurred the lethal phenomena are of such short duration in most cases as to have suggested, we have seen, the term "adrenal apoplexy." In a fair proportion of cases, however, the hemorrhage causes sudden hypoadrenia. The treatment of

this condition is that indicated in the emergency cases of terminal hypoadrenia (see page 413). If the hemorrhage has not been too extensive the chances of recovery will be greatly increased by the use of **adrenal** or **pituitary preparations,** the latter owing its properties, in my opinion, to the adrenal chromaffin substance the pituitary contains. These agents will help to sustain oxidation and metabolism while the adrenal lesion is undergoing resolution.

Although the adrenals have been regarded as impervious to **X-rays,** the writers found that hyperplasia with accompanying overactivity of the glands is reduced by them, owing to a retarding influence upon tissue proliferation. They obtained a reduction of blood-pressure, as shown by Pachon's sphygmo-oscillometer, following irradiation of the adrenals. Out of 16 cases, the pressure remained high in only 1. Zimmern and Cottenot (Arch. d'élect. méd., June 7, 1912).

The writer analyzes the recent literature on hemorrhage in the suprarenals in children. When it is actual apoplexy, it is inevitably fatal, but with anything short of this, with low blood-pressure, intermittent cyanosis and asthenia, large and repeated doses of **adrenalin** are called for, watching over the effect by the arterial pressure. He recalls the interesting case of Vollbach's in which a girl of 15 presented purpura a year before developing Addison's disease. Comby (Arch. de Méd. des Enfants, Dec., 1918).

HEMORRHAGIC PSEUDO-CYSTS OF THE ADRENALS.—
In most instances hemorrhagic blood-cysts are the results of acute hyperadrenia in the course of some infection or intoxication in which the adrenal hemorrhage has been limited to a small area, which eventually develops into a cyst.

SYMPTOMS.—These growths may give rise to no symptoms, other, perhaps, than a sensation of weight, until quite large, when pain supervenes. This is at first indefinite, though most marked in the region of the tumor, in the right or left loin, or in the upper portion of the abdomen and loin. The neuralgia-like pain becomes increasingly severe, and radiates in various directions, especially toward the hip and thigh of the corresponding side, and is subject to exacerbations, which may be very severe, especially after meals. Epigastric pain and vomiting—which affords relief—occur in some cases, especially during these exacerbations of suffering.

While such a cyst or adrenal hematoma may attain a large size, the fact that the opposite adrenal remains uninvolved practically excludes the production of symptoms of altered adrenal function, the signs of the tumor being merely a sensation of weight and pain due to pressure on surrounding sensitive structures. Subsequently, the patient may suddenly begin to fail, losing weight and developing dyspnea, polyuria, hematuria, and even slight bronzing. The termination is usually through rupture into the abdominal cavity. Sajous (Da Costa's Therapeutics, 1918).

The tumor may manifest itself at first merely by enlargement of the abdomen. The bulging then becomes more clearly defined on one side or the other (this variety of growth being almost invariably unilateral), under the lower ribs, which may be pushed outward if the growth is sufficiently large, or below their free border, *i.e.,* between them and the superior spine of the ilium. If the tumor, which grows downward and forward, is sufficiently below the ribs to be palpated, it is usually found globular, or

oval, smooth and tense, though elastic, to the touch. Fluctuation may also be elicited. In some cases it is immovable under palpation, though it may, at first, follow the respiratory movements. Nor can it be grasped as is sometimes possible in renal tumors; if small, the tumor is movable, either upward or downward, but this mobility gradually decreases as the tumor develops. The growth is sometimes sensitive under pressure.

At first, several years, perhaps, the patient may appear normal in every other respect, be well nourished, ruddy, etc. With comparative suddenness, however, he begins to fail, losing flesh rapidly, all the other symptoms mentioned, to which dyspnea and a sense of constriction about the chest is added, becoming more severe. If the cyst does not rupture, polyuria, hematuria, and even slight bronzing may appear. It is probable, however, that this train of phenomena is witnessed only in a very small proportion of cases, rupture and hemorrhage constituting the "adrenal hemorrhage" in adults treated under the preceding heading, being the outcome in practically every instance.

> Adrenal hemorrhage in the newborn is probably not uncommon, but in the great majority of cases there are no symptoms to indicate the occurrence of such a lesion, and the hematoma is quickly absorbed. It is equally difficult to understand why in adults these hemorrhages should occur. The deep situation of the adrenal bodies would seem to be sufficient protection from injury, except that of the severest character, and yet in a certain proportion of these cases the cause has aparently been a trauma. A. J. M'Cosh (Annals of Surg., June, 1907).

[This abstract indicates the drift of the prevailing conception of the pathogenesis of these growths. While local lesions are ascribed to the concomitant disorder, the adrenals, being supposedly affected directly by the toxin or poison that may be present, are thought to explain some cases, others require, it is believed, some form of traumatism. It is to the *excessive blood-pressure produced by the toxin* that the vascular ruptures to which the hemorrhage is due should be ascribed. C. E. DE M. S.]

DIAGNOSIS.—The symptomatology of adrenal cyst, apart from the location of the tumor, does not present, as just shown, very characteristic features. The location of the pain sometimes suggests *intercostal neuralgia;* but inasmuch as pain occurs only when the growth is large, percussion and palpation will reveal the presence of a tumor. In neuralgia the pain is also apt to be localized, thus distinguishing it from the radiating pain of adrenal cyst. The sudden onset of severe pain may be taken for *acute pancreatitis.* The location of pain and tenderness in the upper left abdominal quadrant, the subnormal temperature and the early lethal trend—death occurring sometimes within three days—clearly point to the latter disease. *Pancreatic cyst* is also differentiated by its location and its association with glycosuria, stearrhea, and imperfect digestion of fats and albuminoids. *Hydatid cyst of the liver,* another source of confusion, is attended by the presence of biliary pigments in the urine, the appearance of cysts in the stools and vomited matter, and with obstruction phenomena. *Cancer of the spleen* may be recognized by the more nodular outline of the growth and the cachectic phenomena.

Hydatid cyst of the spleen is usually associated with hydatid cysts elsewhere, and may be accompanied by the presence of hooklets in the excretions. Puncture of the growth should be carefully avoided when there is any suspicion whatever that an adrenal blood-cyst is present. *Renal cysts* are

more easily palpated bimanually, and are usually freely movable.

> Cysts are due to the tendency of the adrenals to hemorrhage. Fourteen cases are reported in literature, of which 7 were *post-mortem* reports or complications of other adrenal tumors. The other cases were well-defined blood-cysts of the adrenal glands. The author reports the case of a waitress with a history of right side pain of a cramping nature, on several occasions—she thought 5 or 6. A large tumor was present in the upper right abdomen; shock, pain, difficult breathing, rapid pulse. Operation showed a cyst covered with peritoneum attached to the back above the right kidney. All organs were displaced by the cyst, which was as large as an adult head. The patient recovered, and was well 1 year later. H. E. Pearce (Trans. West. Surg. Assoc.; Surg., Gynec. and Obstet., Feb., 1917).

ETIOLOGY.—Adrenal blood-cyst has been ascribed to many morbid conditions. Acute intoxications, especially diphtheria, typhoid fever, burns, osteomyelitis, hepatic abscess and tuberculosis, have been regarded as initial factors of these growths, a small cyst formed during the active stages of these diseases, or, as a complication thereof, gradually increasing in size until the foregoing phenomena or adrenal hemorrhage occur. In the light of the data submitted in the foregoing pages, they are merely after-effects or complications, in other words, of the damage done to the adrenals during an acute febrile toxemia.

Atheroma of the adrenal arteries is also regarded, and doubtless justly, as a source of initial lesions, but it is probable that cerebral lesions of the same kind and apoplexy, which have been considered by some authors as etiological factors, are merely concomitant lesions due to general arteriosclerosis.

Thrombosis of the adrenal vein by blocking the efferent circulation has also been incriminated, while traumatism is known to have started the morbid process in at least two instances.

PATHOLOGY.—While older investigators, including Klebs, Virchow and Heuschen, considered these growths as retention cysts, similar to those formed in the thyroid, and thus termed them "struma adrenalis," the prevailing view at the present time is that a small hematoma or an acute congestive process—though erroneously, in my opinion, ascribed to *local* intoxication—initiates the growth. As the latter increases in size the adrenal structure is gradually destroyed and the content is no longer—unless a recent hemorrhage has occurred—merely blood, but a more or less fluid magma of detritus, broken-down blood- and tissue- cells, flakes or fibrin, cholesterin crystals, etc., which may be dirty yellow, greenish or brownish in color. Microscopically, the walls of the cyst, which vary from $\frac{1}{16}$ to $\frac{1}{8}$ inch in thickness, are composed of fibrin tissue; the inner aspect shows shreds or remnants of the adrenal cortex.

Certain thickened portions of the capsule and what semiorganized clots the cyst may contain may be found to include small cysts, chalky deposits. These growths sometimes become very large—as large as an adult head in a case of Chiari's—and contain several pints of blood or liquefied blood and tissue elements.

PROGNOSIS.—The fact that this growth is practically always unilateral, and that the loss of one adrenal does not compromise life, as does removal of both organs, make it possible to remove the growth with safety. The frequent instances of severe collapse and shock

that have followed these operations suggest that the operative prognosis cannot but be improved by resorting to those surgical procedures which will entail the least possible handling of the intraperitoneal organs and of the sympathetic ganglia, all of which are well known to produce shock readily by reflex action.

TREATMENT.—The treatment is, of course, entirely surgical. The cyst may be removed through either an abdominal or lumbar incision. In accord with M'Cosh's advice, which a review of the operative results recorded fully sustains, preference should be given to the **lumbar incision.** The approach is more direct; it avoids the handling of the intraperitoneal organs, which must necessarily take place if the tumor be reached through the abdominal incision, and it affords the most direct route for drainage. In the average case, an oblique incision from behind downward and forward below the last rib, which has been found most convenient for extirpation of the kidney and ureter, is as applicable here. If much space is needed, it is safer to remove the last rib than, as some European surgeons have advised, to resort to the abdominal incision, which, as previously stated, entails considerable shock. The tumor is sometimes found so firmly adherent to the kidney that removal of this organ becomes necessary.

> In the case of large serous cysts complete extirpation should be practised if possible; but if the sac cannot be readily and gently detached from the surrounding parts, the surgeon should rest content with partial resection of the wall of the cyst, and resection of the wall of the cyst. Terrier and Lecène (Revue de Chir., vol. xxvi, No. 9, 1906).
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> A *blood-cyst* filling the entire upper abdomen was successfully removed

by the writer from a woman of 43. This enormous tumor was back of the peritoneum, and its removal was facilitated by tapping, releasing a quart of brownish fluid. The patient convalesced rapidly, although the operation had been long and tedious on account of adhesion of the cystic *adrenal* to adjacent organs. He found 11 cases in the literature with 5 recoveries. Küttner (Beitr. z. klin. Chir., Dec., 1912).

FUNCTIONAL HYPOADRENIA.

DEFINITION.—Functional hypoadrenia is the symptom complex of deficient activity of the adrenals, due to inadequate development, exhaustion by fatigue, senile degeneration, or any other factor which, without provoking organic lesions in the organs or their nerve-paths, is capable of reducing their secretory activity. Asthenia, sensitiveness to cold, and cold extremities, hypotension, weak cardiac action and pulse, anorexia, anemia, slow metabolism, constipation, and psychasthenia are the main symptoms of this condition.

> In a number of examples of suprarenal insufficiency in troops incident upon fatigue, the writers by supplying the lacking adrenal principle, cured the disturbances when they took the form of a diarrhea resembling cholera, as also in grave gastrointestinal toxic infections. The men thus affected had led a sedentary life before the war. Satre and Gros (Prog. méd., June 15, 1918).

SYMPTOMATOLOGY AND PATHOGENESIS.—The process of development in the child and the influence of senility on the adrenals make it necessary to discriminate between the main stages of life, infancy, childhood, adult and old age, in describing this condition.

Infancy.—Although the adrenals are relatively large in the infant (one-

third the size of the kidney at birth), their functions are limited to the carrying on of the vital process, at least during the first year of life, the mother's milk supplying the antitoxic products capable of protecting it against the destructive action of poisons of endogenous and exogenous origin. This protective influence of maternal milk is clearly defined in the following quotation from Professor William Welch's Harvey Lecture: "It is an important function of the mother to transfer to the suckling, through her milk, immunizing bodies, and the infant's stomach has the capacity, which is afterward lost, of absorbing these substances in active state. The relative richness of the suckling's blood in protective antibodies, as contrasted with the artificially fed infant, explains the greater freedom of the former from infectious diseases." Striking proof of this is afforded by the fact that during the siege of Paris, in 1870-71, according to J. E. Winters ("Practical Infant Feeding," p. 6), "while the general mortality was doubled, that of infants was lowered 40 per cent. owing to mothers being driven to suckle their infants."

Childhood.—The predilection of children to certain infectious diseases obviously indicates that it is not only in infancy that vulnerability to these disorders exists; it exposes life during the first decade, and more, of the child's existence. If, then, in the infant the maternal milk, as Welch says, protects the suckling against such diseases, at least to a considerable extent, we must conclude that the same underlying cause of vulnerability persists several years, i.e., until it has in some way been overcome. The adrenals acquire, with other organs, the power to supplant the mother in contributing antitoxic bodies to the

blood; they supply internal secretions which fulfill this rôle.

These facts point to the adrenals as at least prominent organs among those whose inadequate development explain the special vulnerability of children to certain infections, the "children's diseases." It becomes a question now whether there are degrees of this hypoadrenia which render the child more or less liable to infection.

That degrees of hypoadrenia exist in children is, in reality, a familiar fact to every physician when the signs of this condition are placed before him. The ruddy, warm, hard-muscled, heavy, out-of-door, romping child with keen appetite and normal functions, is one in whom the adrenals are as active as the development commensurate with its age will permit. He is ruddy and warm because oxidation and metabolism are perfect and the blood-pressure sufficiently high to keep the peripheral tissues well filled with blood; his muscles, skeletal, cardiac and vascular, are strong because, in addition to being well nourished, they are exercised and well supplied with the adrenal secretion, which, as shown by Oliver and Schäfer, sustains muscular tone. As normal outcome of this state, we have constant stimulation of the functional activity of the adrenals. The muscular exercise and maximum food-intake involve a demand for increased metabolism and oxidation, and the resulting greater output of wastes imposes upon the adrenals, as participants in the oxidation and autoprotective processes, greater work, more active growth and development, with *increase of defensive efficiency* as normal result.

The pale, emaciated, or pasty child, with cold hands and feet, flabby muscles, whose appetite is capricious or deficient—the pampered house-plant so

often met among the rich—represents the converse of the healthful child described, just as does the ill-fed, perhaps overworked, child of the slums. The emaciation, the cold extremities, indicate deficient oxidation, metabolism and nutrition owing to the torpor of the adrenal functions; the pallor is mainly due to a deficiency of the adrenal principle in the blood and to the resulting low blood-pressure, which entails retrocession of the blood from the surface. This child is not ill, but the hypoadrenia which prevails normally, owing to the undeveloped state of its adrenals, is abnormally low, and it is vulnerable to infection.

That all conditions which in the adult tend to produce functional hypoadrenia affect the child at least to the same extent, is self-evident.

Adult Age.—As in the child, the adrenals may be inherently weak. Such subjects do not, as in hypothyroidia, show signs of myxedema; but their circulation and heart action are feeble, they tend to adiposis, and show other signs of hypoadrenia. I have witnessed suggestive bronze spots in such cases. As a rule, however, the development of the adrenals in adults is an accomplished fact—as also that of their coworkers in the immunizing process, the thyroid and pituitary, we shall see. The adrenals, fully capable of sustaining oxidation and metabolism, are able to defend the organism adequately; indeed, they do more: by sustaining oxidation and metabolism up to its highest standard in all organs, they also preserve the efficiency of all other defensive resources, including phagocytosis, with which the body is endowed to their highest level. On the whole, the *normal adult whose adrenals functionate normally is relatively resistant to infection.* The infrequency with which we are infected, notwithstanding daily exposure in our professional work, attests to this fact.

Functional hypoadrenia appears, however, when, irrespective of any disease, and as a result of the vicissitudes of our existence, the adrenals are subjected to abnormal secretory activity.

Fatigue is a prominent factor in this connection. Mosso's ergograph shows clearly the functional efficiency of the forearm. If by means of this instrument we compare the muscular power of a case of Addison's disease with that of any other kind of sufferer, whose muscles are organically normal, a striking difference will be noticed: signs of fatigue appear very soon, and muscular impotence asserts itself where an advanced case of tuberculosis, for example, will be able to show appreciable strength. Intense asthenia is, in fact, a symptom of Addison's disease almost as characteristic as the bronze spots. It is as pre-eminent after experimental removal of both adrenals. This harmonizes with Oliver and Schäfer's demonstration of the influence of the adrenal secretion over muscular tone. Many other proofs could be adduced to show that there is a close relationship between fatigue and the functions of the adrenals. The pale and drawn face of an exhausted man, the readiness with which he suffers from the effects of cold and exposure, especially in the intestines, are familiar features of daily life.

The unusual prevalence of disease among soldiers in the field is, of course, partly due to the defective sanitation that a campaign entails; but fatigue—particularly that due to heavy marching, carrying heavy accoutrements—is, in my opinion, an important predisposing cause, through its influence upon the adrenals. Not only are these organs

called upon to sustain general oxidation and metabolism at a rate exceeding by far that which amply suffices for normal avocations, but the fact that, as shown by Abelous and Langlois (*loc. cit.*), they also serve to destroy the toxic products of muscular activity, constitute another cause of drain upon their secretory resources. "Fatigue," write Morat and Doyon (Traité de Physiologie," Art. "Secretions Internes," p. 441, 1904), referring to experimental fatigue in animals deprived of their adrenals, "has an aggravating influence, as first indicated by Abelous and Langlois, and confirmed by Albanese and all authors. Hultgren and Andersson have even observed sudden death as a result of powerful movements of the body."

Debility from any source, starvation, loss of blood, etc., as efficiently renders the body vulnerable to disease: "Combine toxin and antitoxin, and inject the mixture," writes Professor Charrin ("Les Défenses Naturelles de l'Organisme," p. 63, Paris, 1898); "no harm will follow. But weaken the animal by starvation or slight bleeding and administer the same injection; death will follow with all the signs of poisoning by the toxin, with congested adrenals." , , , "That relations exist between the adrenals and infection," urges the same authority, "is today an incontrovertible fact." It follows, therefore, that hypoadrenia from any source should render the body vulnerable to disease. Deficient food, excessive work, that of the sweat-shops for example, account for much of the predilection of our slums as foci of disease, their filth nurturing the appropriate germs.

Masturbation and excessive venery are important morbid factors in this connection. The pallor and asthenia witnessed in these cases, so far unex-

plained, can readily be accounted for if, as I believe, the liquid portion of the semen is rich in adrenal principle. This is suggested by the fact that spermin, the purest of testicular preparations, gives the same tests and acts precisely as does the adrenal principle. The latter is an oxidizing body acting catalytically; it resists all temperatures up to and even boiling; it is insoluble in ether and practically insoluble in absolute alcohol, and gives the guaiac, Florence, and other hemin tests. Now, spermin not only raises the blood-pressure, slows the heart and produces all other physiological effects peculiar to the adrenal principles, but its solubilities are the same; it gives the same tests; it resists boiling. Moreover, it is regarded in Europe as a powerful "oxidizing tonic," and has been found equally useful in disorders in which adrenal preparations had given good results. The inference that spermin consists mainly of the adrenal product suggests that it should not be regarded as specific to the testes, but, instead, a constituent of the blood at large; not only did this prove to be the case, but it was found in the blood of females as well as in that of males.

Old Age.—Perpetual life would doubtless be ours were it not that all living organic matter is subjected, after more or less precarious periods of growth and adult existence, to one of decline and final disintegration. This applies particularly to the adrenals, if their functions are, as I hold, to sustain oxidation and metabolism, the fundamental processes of the living state. Indeed, the senile state may be said to be as evident in these organs as it is in the features of the aged.

Series of corrosion preparations, of the veins of the left adrenal in different

people, aged, respectively, 22, 30, 80, and 82, using the same injecting substance and technique. They showed conclusively that the vascular system of the adrenals becomes steadily smaller as adult age wanes, being greatly shrunken in old people. Landau (St. Petersb. med. Woch., June 14, 1908).

According to Landau (St. Petersb. med. Woch., June 14, 1908), Ecker, Henle, and von Kölliker found that fat occurred in increasing quantities in the adrenal cortex as age advanced, while Hultgren and Andersson found fibrous tissue between the cortex and medulla in very old animals. Minervini (Jour. d'anat. et de physiol., pp. 449 and 639, 1904) found a similar condition in the medulla of aged individuals. Dostojewski, moreover, observed a marked—occasionally very great—reduction in the size of the adrenals in the aged. Rolleston (Lancet, Mar. 23, 1895) has also called attention to this fact.

Landau studied the influence of age on the vessels, large and small, of the adrenals, adopting for the purpose a process introduced by Rauber and applied by many others, including Bezold, Hyrtl, and Lieberkühn, to the study of other organs, viz., injection of the vessels with some hardening substance, and the subsequent use of a corrosion method to destroy the parenchyma. The adrenals receiving their blood through a number of small arteries, the adrenal vein, which contains no valves, was used for the injection. The annexed plate shows the result. The vessels, and therefore the adrenals, are well developed and in full bloom, as it were, in the adrenals of the three young adults, while those of the aged are shrunken and correspondingly deficient as blood-channels—a certain index of the lowered activity of the adrenal func-

tions, and, through these, of the vital process they sustain.

The asthenia of old age thus finds a normal explanation in the defective supply of adrenal secretion—precisely as it does in Addison's disease. In fact, Rolleston states that atrophy of the glands in the young may produce this disease. Lorand ("Old Age Deferred," Am. ed., p. 111, 1910), in his recently published book on old age, urges, in fact, that "old age is caused by degeneration of the ductless glands, and that there exists a condition of autointoxication in old age" quite in keeping, I may add, with a decline of the antitoxic power shown by the adrenals. Lorand, who has antedated others in showing the influence of the ductless glands upon old age, has found his views confiremed by Campbell (Lancet, July, 1905), Pineles, Sir Herman Weber, and also—though he denies a relationship between old age and myxedema—Metcnnikoff.

In his closing remarks on the causation of old age, Lorand remarks: "It is evident from the above considerations that all hygienic errors, be they errors of diet or any kind of excess, will bring about their own punishment, and that premature old age, or a shortened life, will be the result. In fact, it is mainly our fault if we become senile at 60 or 70, and die before 90 or 100." Hence the motto of his title page :—

"Man does not die,
He kills himself."
                        —*Seneca.*

In the light of the data I have submitted, however, it is clear that the lesions to which the adrenals are subjected during infections and autointoxication, from birth to the last day of life, do greatly shorten it by limiting the functional area of the organs through the local fibrosis they entail. It is quite

probable, in fact, that centenarians owe their prolonged longevity mainly to integrity of their adrenals.

Hygiene, and particularly those of its divisions which bear directly upon the prevention of infectious diseases, thus asserts itself as one of the most useful of our sciences in another direction, viz., that of preserving the organism against those diseases which, seemingly benign because they are recovered from, measles for example, in the end shorten our existence by compromising the integrity of the organs which sustain the vital process itself.

Prophylaxis and Treatment.— Though we are dealing with depraved states of a physiological condition, we cannot but regard them as abnormal in the sense that we deem adynamia abnormal, and, therefore, susceptible to remedial measures. Indeed, there is much that can be done in each of the three forms of functional hypoadrenia described.

In the **infant** we should, by every possible means, prevent infection or intoxication to preserve the integrity of their adrenals and other autoprotective organs. The key of the whole situation lies in the fact that, as Ruhräh states, "nearly all the cases and nearly all the deaths are in bottle-fed babies." Physicians are, as a rule, entirely too ready to yield to the demands of social and other claims put forth by mothers who do not wish to nurse their offsprings. The responsibility assumed by both mother and physician under these circumstances is overlooked. I cannot but hope that if this continues, and the sacrifice of countless infants proceeds, laws may be enacted to prevent it by imposing upon the physician the duty of submitting to the State authorities a certificate in which sound reasons shall alone account for

his consent to a departure from nature's methods which entails deaths untold. J. Lewis Smith states that the death rate among foundlings in New York City reached almost 100 per cent. until wetnurses were provided. Men such as Jacobi, Winters, and many French authorities have written forcibly upon this subject, but seemingly to no avail. The holocaust continues.

Experimental research in the same direction has only served to emphasize the all-important prophylactic value of **maternal milk.** As L. T. de M. Sajous (Univ. of Penna. Med. Bull., June, 1909) states: "That milk is capable of conveying antitoxic substances after these have been injected into the mother has been known for a number of years. In 1892 Ehrlich and Brieger demonstrated this fact in their experiments on mice. The offspring of non-immune mice were suckled by other mice which had been immunized against the actions of certain poisons. It was found that the young were thereby rendered immune to the poisons employed, viz., ricin, abrin, and tetanus toxin. This immunity steadily increased during the period of lactation, persisted for some time after, and then gradually disappeared. Ehrlich thus showed that a passive immunity was created in the young by the absorption of milk from an immune adult, and even went so far as to assert that all so-called heredity immunity was, in reality, of the passive variety, being transmitted during lactation and not inherent in the offspring itself.

"This transmitted immunity has been shown to occur in various other animals. Thus, in 1893, Popoff showed that immunity against cholera could be transmitted through cows' milk. He injected bouillon cultures into the peritoneal cav-

ity of a cow, and later injected into guinea-pigs from 2 to 10 c.c. of the cow's milk. The guinea-pigs become immune against cholera. The same observer noted also that, when the milk was boiled before injecting it, no immunity was produced. Kraus showed that the milk of goats immunized by injections of 'typhus-coli bacilli' and cholera organisms had protective and agglutinating properties. He also ascertained that the relative proportion of agglutinating substance present in milk to that contained in the serum was as 1 to 10. Taking up the subject from the standpoint of tuberculosis, Figari showed, in 1905, that the agglutinins and antitoxins of this disease appeared in the milk of cows and goats that had been actively immunized against it. In another series of experiments he fed the milk of immune cows to a number of rabbits, and in others injected it subcutaneously. In both cases these animals, thus passively immunized, were found to transmit to their young, by their milk, the agglutinins and antitoxins of tuberculosis.

"Evidence is not lacking of the transmission of antitoxic substances through human milk. It has long been known that infants below one year of age were but slightly susceptible to certain infectious diseases, and in particular scarlet fever, diphtheria, measles, and mumps. In fact, it was an attempt to throw some light on this subject that Ehrlich performed his classic experiments on mice in 1892. Four years later Schmid and Pflanz performed some interesting experiments on guinea-pigs. Into some of the animals they injected blood-serum derived from human blood which was taken, at the time of delivery of her child, from a woman to whom had been administered diphtheria antitoxin. Into other guinea-pigs they injected milk from the same woman. The animals were then given injections of the ordinarily fatal dose of diphtheria toxin. From the results obtained the investigators concluded (1) that antitoxin substances found in the blood of parturient women exist also in the milk; (2) that the quantity of antitoxic substances excreted with the milk is much less than that found in the blood. Similarly, in 1905, la Torre injected diphtheria antitoxin in several wet-nurses, and noted the antitoxic power resulting in the blood of the nurslings by injecting measured amounts of this blood mixed with diphtheria toxin into guinea-pigs. He was able to satisfy himself that a passage of the antibodies occurred in small amounts into the blood of the infants.

"These experiments show, then, that antibodies injected into the mother are transmitted to the offspring. This being the case, it is but reasonable to expect that some of the protective substances ordinarily present in the normal mother's blood should likewise reach the child through the milk. Experiments have shown this also to occur. Moro found that the bactericidal power of the blood-serum in breast-fed children was distinctly greater than in those artificially fed. Further confirmation was afforded by the fact that this difference rapidly disappeared when the bottle-fed infants were put back to the breast."

The prevention of disease in the infant is raised to its highest standard by maternal lactation. The organisms of its gastrointestinal canal are kept under control; the barriers to infection that the respiratory tract and pulmonary alveoli offer are well armed with antitoxic bodies; the blood itself is destructive to pathogenic organisms, and the infant is thus protected against those diseases which, even if recovered from, we have

seen, leave enfeebling lesions, fatty and fibrous degeneration, in those organs upon which his health in after years and the duration of his life depend.

In the **child** beyond the nursing period the problem is more difficult. The fatal "second summer" recalls the sins of the milkman, the filth of the cowshed, and of the vessels in which the milk is transported and kept amply long enough to favor the growth of the oft-present Shiga bacillus, the virulent *Bacillus coli*, and even at times the streptococcus. The correction of these and many other factors replete with danger to the child, and which surround it on all sides, offers the only resources to diminish not only the mortality of children's diseases, but their occurrence, besides safeguarding health and longevity in after years. The good already done by our profession in this direction is incalculable. Briefly, public, home, and school hygiene, in the light of the facts I have submitted, not only serves to protect life for the moment when the child is concerned, but its entire career as a healthful individual, while enhancing greatly his chances for a long life.

It now becomes a question whether our resources are such as to enable us to raise, where functional hypoadrenia exists, the autoprotective resources of the child, sufficiently, perhaps, to enable it to resist infection successfully. The influence of many toxins and drugs on the adrenals points clearly to overactivity under their influence. In 1903 ("Internal Secretions," vol. i) I referred to mercury as occupying "a high position among the stimulants of the adrenal system." Now, C. R. Illingworth ("The Abortive Treatment of Specific Febrile Disorders," etc., London, 1888) and others have found the **biniodide of mercury** extremely efficient in aborting

scarlatina, diphtheria, measles, variola, varicella, pertussis, parotitis, and many other infections. The great vogue of **calomel** among the physicians of the past generation may have found its *raison d'être* precisely in just such an action—which I have myself observed. **Arsenic** is a familiar agent in the abortive treatment of malaria in Africa, and, as Surgeon-General Boudin states, in many other diseases. The remarkable results of Petresco with large doses of infusion of **digitalis** in pneumonia have only been tentatively explained. But if we realize that division of the path to the adrenals arrests and prevents the effects of digitalis, as is now well known, there is good ground for the belief that the prevailing conception of the action of this drug is erroneous, and that it is by stimulating the adrenals that it acts, at least in part. In view of the immunizing action of the adrenals, therefore, we can realize how **digitalis** could be of use in this infectious disease, and how it might prove useful in aborting any pulmonary disorder due to pathogenic organisms.

Very remarkable in this connection is the action of **thyroid gland** 1 grain (0.06 Gm.), **adrenal gland** 2 grains (0.12 Gm.), and **Blaud's pill** 1 grain (0.06 Gm.) in a capsule three times daily, previously referred to. Given during meals to a debilitated child of 10 or 12 years, it seems promptly to start the vital machinery on a new lease of life— where, of course, the demands of hygiene are adequately met. **Meat** is of value here, while **milk**, the fluid portion of which gives the test for oxidases, and which, as I have shown elsewhere, depends upon the adrenal secretion for its ferment (adrenoxidase) is also of great value. **Digitalin** or **strychnine** in small doses is added if the heart

is weak or to increase the oxygen in-take. All these agents tend, by keeping up a slight hyperemia of the adrenals (and of the other organs acting in conjunction with it), to augment the efficiency of the child's defensive resources.

In the **adult** functional hypoadrenia may have persisted from childhood. Here the measures just suggested for children apply as well not only as preventives where infection threatens, or as abortive treatment, but also to raise the efficiency of the adrenals and the general health of the individual to the normal plane. It is probable that most tonics exert their beneficial influence through the adrenals. That "tonic" doses of **mercury,** *i.e.,* minute doses, are efficient is well known; we have seen that it is a powerful adrenal stimulant. In toxic doses, in fact, as observed by Moliné (Bull. gén. de thérap., Apr. 8, 1906), it causes intense congestion and even hemorrhage of the adrenals.

While there is no doubt that **meat** in excess is harmful, it is undoubtedly true that, as Lorand (*loc. cit.,* p. 313) states, undernutrition through lack of the necessary proteids in the diet increases the liability to infection, as I several years ago pointed out. Lorand refers to personal cases of tuberculosis arising from a purely vegetarian diet. On the other hand, Richet and Héricourt (Lancet, Jan. 7, 1911) obtained remarkable effects from a diet of raw meat in enabling animals to resist tubercle infection by inoculation, and raw meat has become an important factor in the treatment of this disease. Grawitz (Klinische Pathologie des Blutes, 3d ed., 1906) also found that a purely vegetarian diet predisposed to anemia. We have seen that the adrenals supply the blood its albuminous hemoglobin, a deficiency of which is an important feature of anemia. Did we live where pathogenic bacteria do not flourish, we might safely undertake to adopt vegetarian principles; but a reasonable amount of meat, by keeping our autoprotective organs, and particularly the adrenals, active, serves a very useful purpose.

The influence of excessive fatigue on the adrenals, we have seen, is such as to weaken greatly their functional activity and, therefore, the oxygenizing and immunizing functions of the blood. The main harmful feature in this connection is the *relative* deficiency of rest, which means, from my viewpoint, the inadequate opportunity afforded the adrenals to recuperate. This, of course, should be proportionate to the amount of strain imposed upon these organs, and the resistance of which they are capable. It is probably owing to lack of this that apparently strong men are often the first to "give out" in forced marches. The physical examination being based mainly upon the *status presens*, and the adrenals being necessarily (for we are now dealing with a new line of thought) overlooked as factors, there is marked inequality in the resistance of the men to strain. This applies as well to the pathogenesis of chronic disorders. In a personal analysis of 40 cases of hay fever, for instance, the severity of the disease corresponded to a considerable degree with the number of children's diseases the patient had had, the worst cases having had six of these diseases in comparatively quick succession.

This suggests the need of ascertaining the number and severity of children's and other diseases to which the recruit has been subjected and to add this factor to others in deciding upon his admission to the service or the arm to which he is to be assigned. The

mounted man suffers less from actual fatigue than the infantryman, who must carry his accoutrements, arms, cartridges, etc., aggregating in some armies as much as 70 pounds. When, besides, defective or poor food, impure water, exposure, etc., and other frequent accompaniments of a campaign are taken into account, one need not wonder that disease is a far greater factor as causes of debility and death than wounds.

Briefly, fatigue should be considered, owing to its inhibiting influence on the adrenals and the immunizing process in which they take part, as an important predisposing cause of disease. The periods of rest should be so adjusted, therefore, as to counteract this by far the most destructive factor of active warfare. In civil life, such hardships are seldom endured, but here, likewise, much could be done to prevent infection by means calculated to insure the functional integrity of the adrenals.

To stimulate the adrenal functions when marked fatigue prevails would, of course, only aggravate the hypoadrenia after, perhaps, a period of temporary betterment. The powdered **adrenal substance** should, on the other hand, judging from the effects of injections of adrenal extracts in experimentally fatigued animals, serve a useful purpose.

In **old age** the ductless glands assume such importance that a valuable work has been written by Lorand ("Old Age Deferred," F. A. Davis Co., Phila., 1910) to indicate how the functional activity of these organs could be preserved in order to retard the ravages of age beyond the fifth decade, while prolonging life. The reader is therefore referred to Dr. Lorand's volume for a mass of information which cannot be considered here.

The adrenals, as shown by the plate opposite page 460, are deficient in circulatory activity, and, therefore, unable to sustain functional activity of all organs up to its former standard. It becomes a question whether, realizing this fact, we should by artificial means excite the adrenals to greater activity. That such a step might shorten life instead of prolonging it, is probable. In the first place, the frequent presence of arteriosclerosis in the aged counsels prudence; in the second place, to activate the adrenals would only hasten their degeneration by imposing a greater wear and tear upon them. Drugs capable of enhancing adrenal activity had, therefore, better be avoided in the aged.

Far better is it to *compensate* for the loss of efficiency of the adrenals by supplying to the blood, through a suitable **diet,** substances which contain the adrenal principle. If my opinion that spermin owes its virtues to the adrenal principle it contains is warranted, we can understand why Brown-Séquard rejuvenated himself by means of testicular juice injections (I saw him at the time and can testify to its wonderful effects upon him), since he enriched his blood with the *pabulum* of oxidation, metabolism and general nutrition, without impairing his adrenals. With advanced knowledge we need not follow his example. We have seen that **milk** contains the adrenal principle, and that all animal tissues owe their functional activity to its presence. In milk, **buttermilk** especially (since it is almost pure plasma), we have a ready and inexpensive means to compensate for deficient adrenal activity. If debility and other signs of functional hypoadrenia prevail, I advocate the daily addition to the plain, though varied, diet to which elderly people should restrict themselves of the **expressed juice** (uncooked) of one pound

of **fresh beef** daily, taken in soup, **if** distasteful otherwise, and salted to taste. This is a powerful agent for good which is well borne by the stomach, and which more than compensates for the weakened adrenals, since it rapidly restores strength and vigor—provided, of course, harmful influences in other directions are avoided, and a hygienic mode of life, with reasonable out-of-door exercise, prevails.

In matters sexual, aged men should be extremely reserved, since the waste of seminal fluid to them means waste of life substance, replaced with difficulty and never in abundance.

> Case of total absence of the adrenals in a woman, aged 52, who, in September, 1902, noticed that her hands frequently became cold and discolored. In January, 1903, the joints of fingers and wrists became stiff and swollen; during April she suffered from pleurisy, and one month later noticed that the skin of the entire body was becoming darker (Addison's disease), the abdomen enlarged, and she discovered a slight discharge from the umbilicus. The skin grew darker and darker (scleroderma). The joints of the fingers and wrists became almost immovable and several of the finger-joints ulcerated, attended with a purulent discharge (Raynaud's disease). She suffered intensely with the pain, cold and stiffness in all the joints of the extremities. She became emaciated and the whole integument became dry, hard, and cold.
>
> Under treatment with desiccated **adrenal** immediate improvement was noticed. The ulcerated joints healed, pain in them ceased, and they became more limber. The skin softened and grew lighter. Improvement continued for about one year when the patient complained that the powder disturbed her stomach and refused to continue the drug. From this time she grew gradually worse and the previous ulcerated, stiff, cold,

and painful condition of the joints returned, associated with the increased pigmentation and hardness of the skin. She died suddenly, December 14, 1906. At the autopsy no trace of the adrenals could be found. C. R. Love (N. Y. Med. Jour., Jan. 29, 1910; Jour. Amer. Med. Assoc., Feb. 12, 1910).

PROGRESSIVE HYPOADRENIA.—In this condition, local lesions, tubercular, syphilitic, sclerous, etc., progressively inhibit the functions of the adrenals until they fail, destroying life. *Addison's disease,* treated separately on page 332 of this volume, by Professor J. P. Langlois, of Paris, to whose labors I have repeatedly referred in the foregoing pages, is the most important syndrome of this group. In addition is the group of *malignant tumors* which, though presenting the chief phenomena of the former and, therefore, those of hypoadrenia, include various symptoms peculiar to malignant neoplasms which warrant the recognition of an autonomous syndrome complex.

[A striking feature of tumors of the adrenals is their influence upon sex characters. This is common to many growths regardless of their nature. Thus, a large fibrolipoma of the adrenals among other abnormalities found *post mortem* had produced in a woman of 62 (Tuffier, Bull. de l'Acad. de Méd., May 26, 1914) changes which he described as *adrenal virilism, i.e.,* striking masculine characters. A thick black beard and moustache, a masculine face and voice, great muscular development, with fondness for hard manual labor, digging, etc., and conversion of the clitoris into a penile organ, had all developed gradually since the age of 30. Galais (Société de Psychiatrie de Paris, March 21, 1912) describes 3 similar cases, 2 due to *hyperplasia* and 1 to *epithelioma* of the adrenal cortex. Changes such as the foregoing occur, according to the author, only in the female. Thus while a boy suffering from a sthenic growth, *i.e.,* before the tumor breaks down, may grow

very large, and Herculean muscularly, the sexual organs being as large as those of an adult, which such child may resemble, a girl will undergo similar exaggerated development only for a while, then gradually assume masculine characters such as those described above. A case of hermaphroditism of this type was also described by Auvray (Rev. de gynéc. et de chir. abdom., Apr., 1912) due to an *adeno-angeio-lipoma* of the left adrenal which had attained the size of a cocoanut. Under Hypernephroma in the foregoing pages various examples of the same kind are recorded. C. E. DE M. S.]

CANCER OF THE ADRENALS.

—Primary malignant tumors of the adrenals are generally regarded as very rare, but it is probable that when the symptomatology of these growths will be known by the profession at large, a certain proportion of deaths now attributed to Addison's disease in adults and to asthenic disorders in children will be found to be due to this class of growths. Addison, in fact, included these neoplasms among the etiological factors of the disease which bears his name, but it is now plain that the two syndromes differ in many respects, and that the treatments indicated—medical in the one and surgical in the other—impose the need of recognizing malignant neoplasms of the adrenals as distinct morbid entities.

VARIETIES.—Primary malignant tumors of the adrenals are of the various forms of sarcoma, those most frequently met with and which occur, in the majority of instances, in infancy, childhood and adolescence; *carcinoma,* which occurs, as a rule, in adults or aged subjects. Among the rarer varieties may be mentioned the malignant *hypernephroma* and a class of tumors termed by Prudden *hemorrhagic adenoma.*

The sexes are affected about equally, but they appear much earlier in females than in males. Carcinoma may develop from hypernephroma.

[Sixty-seven collected by Ramsay from literature, including 30 of sarcoma and 37 of carcinoma. This would tend to suggest that the two forms occur about evenly. C. E. DE M. S.]

Primary tumors of the adrenals are very infrequent. In the statistics of the Pathological Institute of Geneva, out of 7249 autopsies performed from Oct. 1, 1876, to Oct. 1, 1903, the proportion was 0.6 of 1 per cent. Dupraz (Revue méd. de la Suisse Romande, Mar. 20, 1906).

Study of the collection of kidney tumors in the Jewish Hospital at Berlin, 103 in all. No less than 69 belong to the group of hypernephromas. In two the writer found unmistakable evidence that true carcinoma had developed out of a hypernephroma. Displaced suprarenal germinal matter had lodged in the kidney in early embryonic existence, a hypernephroma had developed from this, and the carcinoma from the parenchyma of the hypernephroma. The writer does not maintain that embryonal displacement of germinal matter is the only cause of these cancers, but in these cases it was evidently the first embryologic cause, without which these carcinomas would never have developed. The same applies also to some cases of sarcoma developing in a hypernephroma which are in the collection. The sarcoma had developed from the stroma. Neuhäuser (Archiv f. klin. Med., Bd. lxxix, Nu. 2, 1906).

SYMPTOMS.—As a rule, the general phenomena develop insidiously, the adrenal lesion being well advanced when they begin to appear. The strength wanes more or less rapidly; the weight gradually decreases; the pulse and cardiac action become increasingly weaker and more rapid; the temperature shows exacerbation of a couple of degrees at times, but in the advanced cases is usu-

ally subnormal; the appetite decreases; digestive disturbances, such as nausea, vomiting, flatulence and diarrhea, are commonly observed. Anemia is sometimes manifest, the hemoglobin being often reduced to 50 per cent., and the red corpuscles to 3,000,000 or less. Cough, with bronchial râles, localized dullness and hemoptysis are occasional complications, while dyspnea and increase of the number of respirations are apt to occur in advanced cases. The skin may remain normal, but various dedegrees of pigmentation, ranging from slight icterus to actual bronzing, are observed in the majority of cases. The typical facies may alone be present in cases of primary carcinoma.

[This symptomatology is based on a personal analysis of 60 reported cases of primary malignant tumors of the adrenals. The phenomena are clearly explained by the functions I attribute to the adrenals. Being the purveyors of the secretion which—as the albuminous constituent of hemoglobin—sustains oxygenation and metabolism and, therefore, nutrition, increasing emaciation, weakness, hypothermia, the decrease of hemoglobin, etc., are but normal results, all the other phenomena being secondary thereto. The cases in which no pigmentation of the skin occurs are usually those in which but one adrenal is involved. C. E. DE M. S.]

> Case of primary sarcoma of the adrenal glands which did not show symptoms of Addison's disease. The existence of the tumor was not suspected until after the death of the patient. The symptoms present suggested carcinoma of the stomach, though the more characteristic symptoms were absent. Both adrenal glands were sarcomatous. Blackburn (Amer. Jour. Med. Sci., Aug., 1906).

All these phenomena are seldom witnessed in a single case. As a rule, after a period of progressive emaciation and adynamia, a tumor can be detected by palpation posteriorly below the costal margin, close to the vertebral column. The mass at first follows the respiratory movements and recedes under pressure, but it eventually becomes fixed and immovable.

In some cases, especially in infants, the tumor cannot be detected in this manner, but the abdomen gradually enlarges with a steady increase of the line of dullness, though, perhaps, no other symptom be discernible. When the outline of the growth can be clearly followed with the fingers, its border is nodular, as in hepatic cancer, but smooth.

Pain is sometimes complained of; it may be located in the region of the tumor; or, radiating upward or across the back, it may extend to the shoulders.

[The pain has been attributed to the phrenic nerve, but a clearer explanation is the effect of the traction by the tumor, upon the sympathetic ganglia and through the greater splanchnic, upon the sympathetic chain, which is merged in with the mass of nerves, including the brachial plexus, in the tissues of the shoulders. C. E. DE M. S.]

Pressure symptoms are apt to complicate a case of long duration. Ascites, general edema, or edema of the ankles or legs are commonly observed in such cases, due notably, in most instances, to pressure upon the inferior vena cava. Gangrene of the feet has also been observed. In carcinoma metastasis is most common in the liver and lungs; in sarcoma it is not quite as frequent and occurs in most cases in the liver and kidney.

Death may occur suddenly, preceded by very few of the above symptoms, especially the sarcomata of infants. In the majority, however, especially in adults, the morbid symptoms gradually develop and the asthenia increases until unconsciousness, labored breathing and coma terminate in death.

Infants may also suffer from a congenital type of adrenal tumor which simultaneously invades the liver. It is encountered as a congenital tumor during the first week of life. The abdomen becomes increasingly distended; there is moderate emaciation, but no jaundice, pigmentation, ascites, or even pain, the child nursing almost up to the time of death.

> Sarcoma of either adrenal, with metastases in the skull observed in children, shows 2 entirely different syndromes and morbid appearances, according to which suprarenal is the seat of the primary growth. On the left side secondary deposits occur in the liver, in the ribs, and cranial bones, and in the thoracic duct and some of its tributaries. On the right side the primary growth usually attains a larger size, and more frequently remains localized to the abdomen. It tends to involve the kidneys by direct extension into their pelvis, stretching out the kidney substance over it, but as a rule being easily separated. Deposits in the cranial bones often lead to exophthalmos, and this usually occurs first on the same side as the primary growth. Ecchymoses into the eyelids may occur and lead to confusion of the disease with chloroma and infantile scurvy. Frew (Quart. Jour. Med., Jan., 1911).

DIAGNOSIS.—The diagnosis of malignant tumor is not difficult when the tumor is sufficiently large to be discovered by palpation, especially when paresthesia over the kidney is present. This and the asthenic phenomena point clearly to the adrenals, especially if jaundice or any pigmentation of the skin be present. Unfortunately, the morbid process is far advanced, as a rule, when these signs appear. The tumor has been mistaken for *psoitis* and *abscess*. From *hepatic cancer* it differs in that the surface of the tumor is smooth instead of lobulated. Of course, the possibility of metastasis in the liver, its most frequent seat, must be borne in mind. *Hydatid cyst* may be suggested, but the absence of the hydatid thrill and other typical symptoms will avoid error. A projecting and *enlarged gall-bladder* is sometimes simulated by an adrenal tumor capable of displacing the intestines anteriorly; but the latter are much less tense than such a gall-bladder. *Abdominal aneurism* may be suggested, but the absence of aneurismal bruit and the absence of all other signs of adrenal growth eliminate this source of error. In *renal cancer* or *renal hypernephroma* hematuria and other evidences of renal disorder are usually present, while they are more likely to be absent in malignant growths of the adrenals. Pain occurs earlier than in renal tumors, while febrile disturbance is rare in the latter.

> Two symptoms point to involvement of the suprarenal gland: (*a*) paroxysms of pain and paresthesias in the absence of a palpable tumor, and (*b*) a febrile course. The painful paroxysms in renal as well as suprarenal tumors are due to the extension of the neoplasm to the roots of the lumbar plexus. In suprarenal tumor this may occur quite early, owing to the immediate vicinity of these structures. On the other hand, in renal tumors the invasion of the capsule usually takes place at a late period, when the growth has reached so considerable a size as to become palpable. The fact that fever occurs in cases of suprarenal tumors has hitherto been unknown. The writer observed it in 57 per cent. of his cases, while in renal tumors it was present only in 1 to 2 per cent.
>
> Another apparently characteristic fact in differentiating from renal tumor is that the adrenal growth tends to approach more nearly the median line—in the region from the seventh to the ninth costal cartilages; while

the primary tumor of the kidney appears first in the region from the ninth to the eleventh. Tumor of the adrenal at the time of its presentation beneath the margin of the ribs appears broader than does that of tumor of the kidney, and the lower contour of the tumor of the adrenal is much less rounded than is that of the kidney. J. Israel (Deut. med. Woch., Nu. 44, 1905).

[The emphasis laid by Israel on the presence of fever in adrenal malignant neoplasms affords striking proof of the correctness of my contention that the adrenal, through the rôle of its secretion in oxidation and metabolism, was the active organ in fever—a process which pathologists have totally failed to explain. C. E. DE M. S.]

Leucocythemia is sometimes simulated, but the absence of myelocytes and other characteristics soon eliminate this disease.

Ecchymosis of the orbit of unaccountable origin in infants and young children, or tumors of the orbit should cause careful search for other manifestations of malignant hypernephroma of the adrenals.

TREATMENT.—Removal is the only resource, but, as a rule, the result is unsatisfactory, owing to the fact that the presence of the growth is recognized only through metastasis; or when it has developed to a marked extent, and produced either through metastasis, pressure, etc., disorders in other parts of the organism which cannot be reached.

Three cases of adrenal tumor treated by **removal**. One was in a woman, aged 47, on whom the writer operated in 1891, who died of recurrence of sarcoma and exhaustion several months after the operation. The suprarenal growth was so firmly fixed to the top of the kidney that that organ had to be removed as well. The second case was that of a woman, aged 62, on whom he operated in 1897, and who is still living

and well, the tumor removed having been a struma lipomatosa suprarenalis, as described by Virchow. In this case only a wedge-shaped piece from the top of the kidney was removed with the tumor, a procedure followed by no morbid symptom. The third operation, by his colleague, Mr. Ward, was for a sarcoma of the adrenal in a child, aged 12 months. The child died from shock within a few hours.

Of 9 cases, including his own, 5 recovered from the operation and 4 died. The true secret of success lies in operating at an early stage of the growth, as in the writer's second case. Mayo Robson (Med. Press and Circular, Aug. 23, 1899).

Removal of an adrenal myxosarcoma from a man of 50. The tumor weighed about seven pounds when removed. There was no cachexia, mononuclear leucocytosis or other symptoms pointing to the suprarenals. The sound suprarenal must have acted vicariously for the affected organ. The patient had recovered when last seen, two months after a two-hour operation. F. Sicuriani (Riforma Medica, vol. xxi, No. 44, 1905).

Cases in which the tumor involves one adrenal only, as suggested by the absence of symptoms of adrenal insufficiency, marked asthenia, emaciation, hypothermia, etc., and the presence of a tumor and hyperesthesia on one side only, offer a better chance of success, since they indicate that the other adrenal will probably be able to subserve alone the needs of the organism. The chief difficulties encountered in the course of the operation are a marked tendency to hemorrhage, owing to the friability of the morbid tissues.

HYPERNEPHROMA.—This name has been given to tumors formerly considered as lipomata, adenomata or myxomata, but shown by Grawitz in 1883 to be developed from adrenal tissue, either within the adrenals them-

selves or in the kidneys, the walls of blood-vessels or other structures in which "adrenal rests" (fragments of misplaced adrenal tissue) or "aberrant adrenals" occur.

From my viewpoint, these so-called "adrenal rests"—found in 90 per cent. of all autopsies by Bayard Holmes, at least once a week by Grawitz in his autopsies, etc.—are not misplaced fragments of adrenal tissue; they belong normally to the kidney.

[I have shown (Monthly Cyclo., June and July, 1909) that what has been termed the internal secretion of the kidney is a product the properties of which correspond with those of the adrenals, and (see "Internal Secretions," 3d ed., p. 289, 1908) that the kidney and the adrenals were governed by the same nervous structures, being thus closely linked functionally. Under the influence of centric impulses the so-called adrenal rests and the adrenals are both caused to increase their secretory activity and to enhance the intrinsic metabolism of the tissues they supply. On the whole the "adrenal rests" are but local aggregates of the chromaffin substance found in all sympathetic structures. C. E. de M. S.]

Study based upon 48 hypernephromata. Thirty-four of the tumors were removed at operations in the Mayo Clinic, and 14 were unreported cases gathered from outside sources. The following general conclusions are drawn from this study: 1. Most, if not all, so-called "adrenal rests" are probably of Wolffian origin. 2. There is almost no evidence, embryological or histological, in support of Grawitz's hypothesis that the so-called hypernephromata have their origin in adrenal rests. 3. There is much evidence that the so-called hypernephromata do arise (according to Stoerk's hypothesis) from proliferations of the adult secreting epithelium of the convoluted tubules. 4. There is much evidence that the so-called hypernephromata do arise from islands of nephrogenic tissue (primitive renal blastema). Such tissue is sometimes present in the adult

kidney and appears capable of forming tumors of non-infiltrating mixed cordon, tubular, papilliform, and sarcoma type characteristic of the so-called hypernephromata. L. B. Wilson (Jour. of Med. Research, Jan., 1911).

Hypernephromas are relatively common in the kidney, constituting, as shown by Albarran and Joubert, 17 per cent. of all renal tumors; they are much less frequently found in the adrenals proper, or in other organs, such as the uterus, ovary, the broad ligament. Microscopically they present the typical characters of the adrenal cortex, and closely, as a rule, infest vascular channels. These vessels and adjacent tissues usually contain a colloid material similar to that found in the thyroid, or secreted by the adrenals. They are benign at first and become troublesome— sometimes after many years—mainly on account of their size, which sometimes reaches that of a child's head, but the pressure they exert on surrounding structures, their tendency, even when benign, to metastasize in the lungs, bones, brain, give them their malignancy.

SYMPTOMATOLOGY. — Before the local symptoms of the tumor appear —when any are clearly discernible—it evokes phenomena which are diametrically opposed to those of Addison's disease, and which correspond with increased nutrition and a stimulation of growth such as that produced by thyroid preparations in cretinism.

[This action on growth and its resemblance to that brought about by thyroid overactivity has imposed itself upon investigators quite independently of my own view—advanced in 1903 ("Internal Secretions," vol. i, pp. 146-152), that it was in great part through the adrenals, i.e., through incidental stimulation of the adrenal center by the thyroid secretion, that

the benefit of thyroid in cretinism was produced. The confirmatory evidence it affords is self-evident. The excess of adrenal tissue which constitutes hypernephroma brings about the general phenomena of overnutrition merely because it awakens excessive metabolism precisely as if the thyroid overactivity had done so by exciting the adrenal center. C. E. DE M. S.]

The symptomatology varies considerably in different cases and suggests that several types exist which our present knowledge does not enable us to discriminate. Some of these exhibit such malignancy that they have been grouped in a separate class. Beginning with hypernephromas of the adrenals proper, we will first review this class of cases.

MALIGNANT HYPERNEPHROMA OF THE ADRENALS.—

This growth occurs, as a rule, between the first and eighth year, especially in girls of the latter age, and causes premature development so marked, in some instances, that the child appears, as to size and development, twice or three times its true age. The face, genitalia, and pubis are covered with abundant growth of hair, the external genitalia being as fully developed as in the adult. The body is obese, the appetite and thirst excessive, although gastric disorders, including stubborn vomiting, are common. The skin may be swarthy or dark-hued, as in a brunette, but not bronzed as in Addison's disease. Such children are usually cross and sullen, unlike obese children, in whom the obesity is due to deficient fat catabolism. These primary growths of the adrenals, which are usually observed in girls, are of slow development, and years usually elapse before metastasis and pressure phenomena—those which give the growth its malignancy—appear.

The abnormal growth of the child may suggest gigantism or acromegaly,

due to some disorder of the pituitary body, but the characteristic growth of the extremities, the absence of obesity in these disorders do not occur in hypernephroma. An elevated temperature is often observed in these cases.

[The occurrence of fever in these cases is clearly accounted for by my views. As shown in "Internal Secretions" (vol. ii, p. 1907), the pituitary body contains the sympathetic center besides the adrenal center. During the first or erethic stage, therefore, the adrenals, the secretion of which sustains oxidation and metabolism, and which alone cause overgrowth in malignant hypernephroma, are not alone overactive, but the arterioles, which the sympathetic governs, also. The blood is not only abnormally rich in oxygenizing properties, therefore, in this disease as it is in malignant hypernephroma, but it is also driven with excessive energy into the tissues, particularly in the long capillary loops of the extremities. Hence the difference between the phenomena of overgrowth in the two diseases and the elevated temperature. C. E. DE M. S.]

Hypernephroma, whether in the adrenal or in the kidney, contains considerable adrenal tissue, usually of the cortical type. It may provoke sexual phenomena.

A study of 17 collected cases, showed that abnormal sex characters do not always attend adrenal hypernephroma. In children they are almost invariably present in the form of hirsutes and often other abnormalities. In adult females before the menopause they are frequently present. In females after the menopause none is recorded, excepting a growth of hair on the face or change in the voice. In adult males they are probably absent. Adrenal cortical rests or bilateral hyperplasia of the adrenal cortex was noted in 15 per cent. of female pseudohermaphrodites, but in only 0.7 per cent. of male pseudohermaphrodites. According to the authors, there is no evidence that hypernephroma in the kidney, which

Appearances of kidney and tumor on section through the long axis of the organ and its pelvis. (Annals of Surgery, Dec., 1906.)
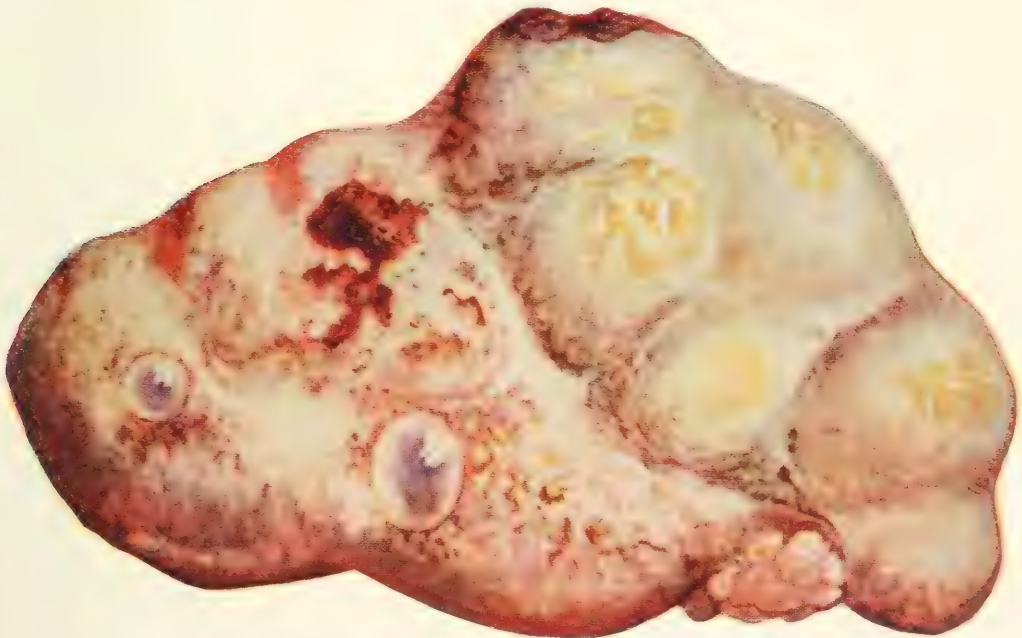
Hypernephroma. Showing the external appearance of the kidney and tumor about one-third smaller than at the time of operation. (Annals of Surgery, Dec., 1906.)

shows a totally different histological structure from that in the adrenal, is ever associated with abnormal sex characters. Glynn and Heidetson (Jour. of Path. and Bact., July, 1913).

Case of a boy in whom the sexual development began at about 18 months. At 10 months he could talk well; at 3 years his voice was that of a man; he had hair on the face and pubis, and was very strong and active. At 5 years and 10 months his facial appearance was that of a man of 35 or 40. Death followed soon after, the autopsy showing a large adrenal tumor. J. F. Baldwin (Jour. Amer. Med. Assoc., Dec. 26, 1914).

A case of hypernephroma showing small tumor in the anterior lobe of the pituitary and another in the left adrenal medulla with hyperplasia of the cortex, was described by the writer. While the adrenal lesion was suggested by marked hair growth, petechial hemorrhages on the hands and arms which became more generalized and grave, those of the pituitary (asthenia) marked adiposis, extreme headaches, slight exophthalmos, pain behind the eyeballs, insomnia, with ultimate death from asthenia. The author lays stress on the need, owing to the interdependence of the various ductless glands, of taking into account a polyglandular syndrome. J. Anderson (Glasgow Med. Jour., vol. lxxxiii, p. 178, 1915).

Case in a girl of 3 years, in which a large, hard, retroperitoneal tumor could be felt in the left abdomen. Fever and increasing asthenia were also present. The child was some 5 inches above the normal, and her physical characteristics, especially the genital organs, were those of an adult. Death followed operation. A large adrenal tumor was found *post mortem*. Out of 15 cases found in literature by the author, the tumor was on the left side in 12. Van den Bergh (Nederl. Tydschr. v. Genesk., Nov. 13, 1916).

Infants and young children are also subject to a form of primary malignant tumor of the adrenals, described by Hutchinson, in which, even before the neoplasm, which grows with great rapidity, can be felt in the renal region, there appears a spontaneous—sometimes traumatic—ecchymosis of one or both eyelids, soon followed by (usually unilateral) exophthalmos and metastasis in the skull, and often in other bones, especially the ribs. The pre-auricular lymph-nodes, and those behind the angle of the jaw, are enlarged, and the whole temporal region eventually becomes the seat of a malignant growth. Pain in this location and optic neuritis with amblyopia may complicate the case. Death occurs early from anemia and cachexia.

Out of 196 cases of kidney tumor 146 were hypernephromata—that is, almost exactly 75 per cent. The remaining 25 per cent. are made up mostly of sarcomata, to a much less extent of squamous epitheliomata of the pelvis, while a true carcinoma of the kidney, apart from hypernephroma, is a very great rarity, or, possibly, does not exist. The kidney tumors of children are practically all sarcomata; there is but one case on record of a true hypernephroma in an infant, and, as was long ago pointed out by Küster, malignant disease of the kidney is a disease of earliest childhood and middle age, affecting but little young adults and the aged. We may conclude that hypernephroma is the common kidney tumor of adults, and that any given kidney tumor in an adult is much more likely to be one of this type than anything else. Trotter (Lancet, June 5, 1909).

Adrenal carcinoma shows two entirely distinct syndromes and pathological states, according to which adrenal is the seat of the primary tumor. On the left side secondary deposits occur in the liver, ribs, cranial bones, and in the thoracic duct and some of its tributaries. On the right side the primary growth generally attains a larger

size, and oftener remains localized to the abdomen. It tends to involve the kidneys by direct extension into their pelves, stretching out the kidney substance over it, but, as a rule, being easily separated. Secondary deposits occur on the upper surface of the liver, in both lungs, occasionally in the cranial bones, and also in the right lymphatic duct and some of its branches. The lymphatics of the right suprarenal are tributaries of the right lymphatic duct, and do not, as is usually stated, follow a course similar to that of the lymphatics of the left adrenal, viz., join the lumbar glands. Deposits in the cranial bones often cause exophthalmos, this usually occurring first on the same side as the primary growth. Ecchymoses into the eyelids may occur and lead to confusion of the disease with chloroma and infantile scurvy. The tumor in these cases involves the medulla of the adrenal, and there are reasons for believing that it is of carcinomatous nature. No pigmentation or evidence of a premature sexual development, such as have been described as occurring in cases of carcinoma of the cortex of the suprarenal, were found in any of the cases studied. R. S. Frew (Quarterly Jour. of Med., Jan., 1911).

HYPERNEPHROMA OF THE KIDNEY.—It is to renal growths developed from the so-called "adrenal rests" that Grawitz, in 1883, gave the name "hypernephroma." They occur not only more frequently in the kidneys than elsewhere in the body, but constitute a large proportion of all renal tumors, i.e., 17 per cent.

SYMPTOMATOLOGY.—Hematuria is often the first and the most frequently observed symptom of renal hypernephroma, having been noted in 90 per cent. of all cases. The hemorrhages are usually severe and occur intermittently, weeks and even months elapsing between them. Worm-like clots—thus shaped during their passage through the ureters—are often passed. During the

intervals the urine is either clear or it may contain red corpuscles. The hematuria is increased by exercise and by manipulation of the region overlying the growths if the latter is sufficiently large to be felt. It may be the only symptom of the growth or precede the detection of the latter by palpation as much as ten years. As a rule, however, the tumor (which occurs in 80 per cent. of all cases) is sufficiently large to be detected much earlier, and sometimes immediately after an attack of hematuria. It is located in the loin, often on the right side, and two or three fingerbreadths below the costal margin. It is at first small—about the half of a walnut—and is movable in about one-half of the cases. As a rule, palpation causes no pain at first, though it may prove tender when directly pressed upon.

Dull pain in the lumbar region, suggesting lumbago, may be the initial symptom. This pain gradually increases and, after being centered in the region of the growth, with a sensation of weight, increasingly radiates in various directions, the back, the abdomen and the testicles. It may come on suddenly and last three or four hours, then be followed by hematuria and frequent urination, followed by a period of rest, during which the urine is slightly albuminous. The urine sometimes contains a few casts, oxalate of lime and a few corpuscles. During this period of rest a certain stiffness may be experienced on the side of the tumor. Varicocele is frequently observed in these cases, on the same side as the focus of pain; it may develop simultaneously with the latter and disappear when the patient assumes the recumbent position.

While periodical hematuria, a tumor and pain in the locations mentioned are typical signs of renal hypernephroma,

other phenomena may appear gradually as the morbid process advances. Most important among these are the metastases, which occasionally occur at first signs of the disease. This is especially the case in bone metastasis, which may appear in the vertebræ, the ribs and other long bones, the skull, scapula, etc., *i.e.*, practically any portion of the skeleton. Metastasis may also occur in various viscera, particularly the lungs, the consolidation in the latter suggesting the corresponding stage of phthisis.

> Case of renal hypernephroma in which the first evidence was a metastasis in the upper part of the humerus, the only sign of the primary growth being an enlargement of the left kidney. Fifteen cases from literature suggested the following deductions in this connection: 1. A bone metastasis may be the first sign of hypernephroma. 2. A bone tumor in a middle-aged or elderly person should suggest a metastatic hypernephroma, for a primary bone tumor in elderly people is uncommon. 3. The bone metastasis from a hypernephroma may be the only metastasis. 4. A hypernephroma may exist for a considerable period without symptoms. 5. The kidney region should be palpated with great care in every case of bone tumor. C. L. Scudder (Annals of Surg., Dec., 1906).

A remarkable case was observed by the writers in a girl, who had begun to show growth of hair on the pubis at 1 year, and developed bodily very early. At the age of 7 there was a profuse growth of hair on the pubis, in the axillæ, on the chin and upper lip. The skin of the abdomen and legs was rough. She was mentally precocious and remarkably strong. Her voice was coarse and deep. The clitoris was an inch long, half an inch in diameter, and notched on the under surface, suggested hypospadias. An abdominal tumor was discerned in the right hypochondriac region, without enlargement of the super-

ficial lymph glands. At operation an enormous perivascular and adherent hypernephroma of the right kidney was removed, with death 3 hours after operation. The tumor occupied nearly the entire abdominal cavity. The uterus and ovaries were infantile. The left kidney and adrenal appeared normal. The lungs showed a moderate degree of metastasis. Microscopic examination of the tumor showed hypernephroma, with much tissue of the type of the adrenal cortex. No right adrenal body was found.

Reviewing other cases previously reported, one of the authors notes that of these 18 cases, 14 were girls. One can differentiate these cases from true sexual precocity in girls by the presence in the latter condition of menstruation, enlargement of breasts and retention of female characters; and from similar conditions in boys by the development of the penis and testes. All of the 18 cases died before the 16th year. Exploratory operation should be done early, even before a tumor is palpable; with a tumor present, removal is imperative. H. D. Jump, H. Beates, and W. Wayne Babcock (Pediatrics, July, 1913).

Only 43 cases of occlusion of the inferior vena cava by a new growth have up to the present been accurately described. In 13 of these the growth reached as far as the right auricle or actually invaded it. In the writer's case, a renal hypernephroma extended from the kidney into the left renal vein, traversed the inferior vena cava below as far as the iliac bifurcation and grew upward into the right auricle and right ventricle, causing mechanical embarrassment of the tricuspid valve. The orifices of the hepatic veins were plugged with the tumor, and there was acute central necrosis of the liver from thrombosis of the hepatic vein and its branches. Sudden enlargement of the liver was accompanied by the onset of acidosis, which continued until death, 24 hours later. Jacobson and

Goodpasture (Arch. Internal Med., July, 1918).

[When adrenal tumors are sufficiently large to be recognized by physical examination they have usually begun to break down, the case passing from the sthenic stage, when the signs are those of *hyperadrenia* to the asthenic stage, when the phenomena of *hypoadrenia* appear: asthenia, low blood-pressure, yellow or bronze pigmentation, dyspnea, cyanosis, etc., along with whatever symptoms the causative tumor may itself awaken. C. E. DE M. S.]

The arteries may be thickened and show clearly defined signs of arteriosclerosis, quite in contrast, sometimes, with the relative youth of the patient, and the blood-pressure be quite high. The skin is not bronzed in these cases, but yellowish, and sometimes swarthy or smoky, this being replaced by pallor when the end is near. The temperature may be raised, but this rarely exceeds 1° or 2° F.

[An important feature in this connection is that bronzing is a characteristic of *insufficiency* of the adrenals, as in Addison's disease, whether due to degeneration, tuberculosis, or malignant tumor of these organs or of their nerve supply. In hypernephroma, on the contrary, we have an addition of adrenal substance to the circulation through the secretory activity of the adrenal rests, as shown by the familiar results of adrenal overactivity enumerated —high blood-pressure and arteriosclerosis. The icterus or swarthiness here is due, from my viewpoint, to the continuously high blood-pressure which causes the cutaneous capillaries to become hyperemic and to expose an increased quantity of the adrenal principle—the component of melanin (see "Internal Secretions," vol. ii, p. 835) to oxidation. The stage of bronzing is not reached because the pigment is not deposited in the cutaneous tissues, as it is in Addison's disease, but merely supplied to them in excess. C. E. DE M. S.]

The duration of the disease varies from fifteen weeks to eight years. The patient gradually loses flesh and grows weaker, all the symptoms become aggravated, hematuria becoming prominent, causing marked secondary anemia; moderate edema of the lower limbs may appear mainly as a result of pressure on some large venous trunk, and delirium sometimes precedes the terminal coma.

DIAGNOSIS.—The pain in the region of the affected kidney, the hematuria accompanied by frequent urination and the localized tumor, are the chief diagnostic points among those previously enumerated, but other features may serve to facilitate the diagnosis. Gellé pointed out that fragments of the tumor, which is very friable and often dissociated during hemorrhages, could be found in the clots passed with the urine. The cells preserve their characters and staining properties.

As to diagnosis of the tumor itself after removal, Croftan found (1) that a watery extract of fresh hypernephroma, in keeping with adrenalin and adrenal extracts, provoked glycosuria when injected in the rabbit; (2) that a pure starch solution, to which the watery extract of hypernephroma was added, contained an appreciable quantity of dextrose; and (3) that the watery extract also possesses the power to decolorize an iodine starch solution. These simple tests make it possible to differentiate hypernephroma from other tumors of the kidney. This is important, since the post-operative prognosis of hypernephroma is much more favorable than that of any other malignant tumor of the kidney. A high blood-pressure tends greatly to insure the diagnosis.

There are no pathognomonic signs of renal hypernephroma. A diagnosis, especially in the early stages, must be made by a process of exclusion. Two personal cases, one of which was a boy of 14, showed ex-

tensive arteriosclerosis. This suggests again the importance of blood-pressure determinations in all cases where a suspected kidney lesion exists. Hematuria is the most important early sign. Metastasis occurred in three instances as late manifestations. Only two of the eight cases were operated upon. They have remained well seven and fifteen months respectively. H. C. Moffitt (Boston Med. and Surg. Jour., Oct. 8, 1908).

A question in regard to these cases which has never been thoroughly investigated is that of increased arterial tension. It is logical to suppose that, with an increase of adrenal tissue, we may have an excess of adrenal secretion, which would result in a rise of blood-pressure—certain writers have noted that this was true; but observations upon this point sufficient to settle the question have not yet been made. Every case of hypernephroma should be thoroughly investigated in this regard, and we may find that a study of the blood-pressure furnishes us a valuable aid in diagnosis. George E. Beilby (Albany Med. Annals, Jan., 1909).

Various disorders may be suggested by hypernephroma, prominent among which is *urinary calculus*. In this connection the pain is coincident with the hemorrhage, while in hypernephroma the pain continues after the latter, though greatly relieved. The vermicular and cylindrical shape of the clots in hypernephroma is also suggestive. Cystoscopic examination at this time often reveals these clots projecting from the ureter of the diseased kidney, whose tumor can also, in some instances, be discerned under X-ray examination. *Pregnancy* is sometimes suggested when the growth projects anteriorly, especially in view of the fact that amenorrhea sometimes precedes the abdominal enlargement.

Hypernephroma may be mistaken for *enlarged spleen*. The latter is usually

nearer the surface and its mobility on inspiration more marked. It is located on the left side, whereas hypernephroma, in most instances, occurs on the right side. Catheterization of the ureters may serve to indicate, between the periods of hematuria, which of the two kidneys is most impaired functionally. The blood count affords little, if any, information, any diminution of red corpuscles—sometimes to an extreme degree—being readily accounted for by hematuria. Moderate leucocytosis occurs in some cases, but not with sufficient frequency to give this sign any diagnostic importance.

In some cases the symptoms and physical signs, other than hematuria, afford but little help to establish the identity of the tumor, either anteriorly or posteriorly. In that case the absence of pregnancy being clearly established, an exploratory incision followed immediately, if hypernephroma be present, by its radical removal, is indicated.

PATHOLOGY. — Hypernephroma is usually located in the upper pole of the kidney, immediately, therefore, under the adrenals. When found early in life at autopsies hypernephromata may be no larger than lentils, or even smaller, but they may attain the size of a child's head, growing outwardly, or, in some cases, inwardly, at the expense of the renal tissues. They reproduce more or less perfectly, the adrenal tissue, the smaller growths being made up, as a rule, of the cortex, and the larger of both the cortical and the medullary substance. They are firm when small, but when they attain a certain size their tendency is to become lobulated, the projecting masses becoming softer and cyst-like. They are lobulated owing to the fibrous bands derived from the renal capsule, and the lobules, when opened,

may be yellowish, grayish red, or brown or blackish, and contain hemorrhagic areas—the source of the blood which causes hematuria.

[The various colors mentioned correspond suggestively with the cutaneous pigments I have ascribed to the adrenal principle in icterus bronzing, etc., and this, in turn, further confirms the fact that the melanins are mainly composed of this principle ("Internal Secretions," vol. ii, p. 835). Hence the association of hypernephroma with melanotic sarcoma by various pathologists. C. E. DE M. S.]

The larger growths are those which tend to become malignant and to produce metastases. These occur through the blood-vessels, both the arteries and veins; the bones and lungs, as previously stated, are the structures most frequently invaded, though, occasionally, extension occurs by the lymphatics, including the retroperitoneal glands.

Microscopically they usually contain a scanty stroma composed of vascularized connective tissue in columns and a parenchyma formed of endothelial polygonal or columnar, translucent nucleated cells, which differ entirely from those of the renal epithelium. The cytoplasm is granular and contains, besides detritus and giant cells, numerous fat-laden vacuoles. It is the presence of considerable fat which first caused these tumors to be regarded as lipomata. The fat contains lecithin. Glycogen is also present, sometimes in relatively large quantities

Prior to 1883 many forms of renal growths were grouped under the head of lipomata. Some authors had previously, and others since that time, described these neoplasms as adenomata arising from the renal tissue itself, Grawitz was the first to bring order out of chaos when he maintained that these growths formerly described as lipomata in reality had their origin in suprarenal tissue misplaced within the kidney. His reasons for believing these tumors to

be of adrenal origin were: (1) the subcapsular position in which aberrant adrenal tissue is likely to occur; (2) the cells were quite different in form from the renal cells, and contained fat-globules in large drops like fatty infiltrated liver-cells; (3) the capsule and the arrangement of the tumor-cells in rows, like the suprarenal cortex, the preponderance of cells over stroma; (4) amyloid degeneration of blood-vessels present in his case only in the adrenals. Others, like Chiari, Lubarsch, and many others, supported Grawitz's views and added the following criteria: (1) the similarity between tumors of the adrenal body itself and these growths; (2) the presence of glycogen. The frequency with which portions of the suprarenal tissue are found under the true renal capsule and imbedded in the renal cortex was shown to be astonishingly great by Grawitz. L. L. McArthur and D. N. Eisendrath (Phila. Med. Jour., April 29, 1899).

Four personal cases illustrating the stages of transition from the smallest benign neoplasm, a pure aberrant adrenal germ to the large growth which assumes the characteristics of a cancer.

Gradually as the malignant growth is approached, the adrenal germs or "rests" lose their normal characters to assume the vague embryonic cellular types. These correspond in every way with the renal cancers containing translucent cells which certain classic writers still consider as renal cancers, but which in reality are hypernephromata. E. Gellé (L'Echo méd. du Nord, Aug. 2, 1908).

PROGNOSIS.—As a rule, hypernephromata grow slowly at first, months, and even years, elapsing before they metastasize or show other signs of malignancy. They may then progress very rapidly, and, the hematuria becoming continuous, death occurs from exhaustion.

A case was reported by Hausemann in a woman 60 years of age, in whom the tumor had been present fifteen years without evidence of rapid growth.

Suddenly the tumor began to grow rapidly and the hematuria which until then had been periodical and not profuse, became continuous. The patient died of exhaustion within a few months. Kusmik (Beiträge zur klin. Chir., Bd. xlv, S. 185, 1905).

They show a tendency to recur, though years may elapse before recurrence occurs. If recognized early, however, removal affords a greater chance of permanent recovery.

Out of 4 cases, 1 of the patients already reported was known to be well seven months after operation; another has remained well fifteen months, but the presence of a varicocele on the sound side renders his future doubtful. Dr. Levison operated on a second case that remained well for some years. Out of 24 cases with operation recorded by Albrecht, 8 died from the immediate results of the procedure and 9 soon afterward from local recurrence or metastases; 1 died of pneumonia two years after operation, and autopsy gave no evidence of recurrence. Only 4 patients remained well after three years, and of these 1 developed metastasis in the occipital bone at the end of four years; a second, metastasis in the scapula after four years and three months; a third, metastasis in the spine after seven years. Only 1 patient out of the 24 remains well after four years. The danger of metastases years after operation renders prognosis most uncertain. Claimont has recorded a case of recurrence in the bronchial glands ten years after removal of a renal hypernephroma. It must be remembered, however, that Albrecht has shown that there may be but one metastasis, and removal of this may lead to a permanent cure. The disheartening results of operations in the past should spur on the clinician to try all methods that may lead to early recognition of the growths. H. C. Moffitt (Boston Med. and Surg. Jour., Oct. 8, 1908).

TREATMENT. — An **exploratory incision** is warranted, as previously stated, when an abnormal growth in the abdomen or in the region of the kidney occurs coincidently with hemorrhage, even when other symptoms of hypernephroma are not present. The majority of authorities consider this procedure advisable even when hemorrhage into the bladder cannot be accounted for. In some cases discomfort or tension over one kidney, and deep comparative palpation on both sides may suggest which side should be explored first; but if this unilateral examination fails to indicate the presence of a growth, exploration of the other kidney is justifiable. In some instances the organ is merely enlarged, especially toward the upper pole, or at the hilum. **Removal** of the growth may be performed extraperitoneally through a lumbar incision. The fatty capsule should, according to Kuzmik, be removed along with the growth, as it may be infiltrated and thus lead to recurrence.

Case in a woman aged 37, married, who had an abdominal swelling the size of a fetal head at term. It was very mobile and fluctuant, and could not be pushed down into the pelvis. A diagnosis of cyst of the kidney or ovarian cyst with a long pedicle was made. On opening the abdomen the tumor was found to be retroperitoneal and crossed by the descending colon. The peritoneum was divided and the cyst enucleated. There was no pedicle. The cyst lay immediately in front of the left kidney, which was normal. The patient made a rapid recovery. On section the tumor contained blood and clots. The cyst-wall showed fibrous septa inclosing polyhedral granular nucleated cells, closely resembling the "zona glomerulosa" of the normal suprarenal capsule. Archibald Donald (Brit. Med. Jour., Dec. 9, 1899).

Two cases of hypernephroma, both of which were absolutely well one year after operation, a **nephrectomy**

having been done at that time. Keen, Pfahler and Ellis (Amer. Med., Dec. 17, 1904).

An extraperitoneal operation can be done even for the removal of a very large tumor, although it is possible only when the tumor has slowly grown into the tissues of the mesocolon, and the ventral or right peritoneal surface of the colon has become greatly hypertrophied or enlarged, and the blood-vessels of the colon so distorted that a long incision would not, in any way, vitiate the blood-supply of this large duct. The results of a personal operation also showed the necessity of taking advantage of every opportunity to completely remove a neoplasm, no matter how grave the prognosis may be at the time of operation. Bayard Holmes (Med. Standard, Nov., 1904).

Case of hypernephroma of the left kidney in which the following proved successful: the patient having been perfectly well fifteen months before the present report. A Morris incision on the left side began about 2 cm. outside the quadratus lumborum and extended forward and downward to the level of the anterior superior spine. This necessitated division of the external oblique muscle. The peritoneum was pushed forward and the kidney tumor removed after much difficult dissection. The tumor and kidney measured 18 x 10 x 8 cm., and was densely adherent at the upper border. The vessels were ligated high up, and on account of the high position of the tumor the tips of the tenth and eleventh ribs were divided subperiosteally and the diaphragm raised with retractors. Most of the capsule was removed and the ureter was stripped downward, almost to the bladder, and cut short after carbolizing the end. The vessels were large, but not occluded by the tumor mass, and were ligated by Pagenstecher. The peritoneum was opened at the upper end of the incision, but was easily closed with continuous catgut sutures. The hemorrhage was fairly severe from the capsule, but was readily controlled. The remnant of the capsule was stitched with catgut and a cigarette drain inserted in the space. Muscles sutured with chromicized gut, skin with silkworm gut and continuous plain catgut. Sterile gauze dressing. H. C. Moffitt Boston Med. and Surg. Jour., Oct. 8, 1908).

C. E. de M. Sajous,
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ADRIN. See Animal Extracts: Adrenals.

AGALACTIA. See Mammary Gland.

AGAR-AGAR is the East Indian name of a substance extracted from various seaweeds, which is available in the shops in the form of long, transparent strips resembling goose-quill pith, and also in quadrangular cakes weighing about 150 grains (10 Gm.) each. It consists chiefly of gelose, and is soluble in hot water, though insoluble in cold water. It has been extensively used as a culture medium and as a demulcent, combined with glycerin for **chapped hands** and **lips.**

Recently, however, it has been used for **constipation** in doses ranging from 1½ drams (6 Gm.) to ½ ounce (8 Gm.), coarsely comminuted and mixed with food. It becomes a jelly in the stomach and intestines by absorbing water and, being indigestible, gives considerable bulk to the feces, thus promoting defecation mechanically. A. Schmidt gives agar-agar cut up in small pieces, adding 25 per cent. of an aqueous extract of cascara sagrada. One teaspoonful to a tablespoonful in mashed potatoes or any other soft food is given daily in chronic constipation.   S.

Pads of agar, or agar tied in the center of a square of gauze, are recommended for the dressing of wounds, being very compressible and elastic. It absorbs 8 times its weight of water, and dries extremely slowly, while microbes and leucocytes accumulate in it. Loeper and Barbarin (Paris Méd., Sept. 23, 1916).

AGARICIN is obtained from the white agaric (*Boletus laricis*), a fungus growing on the trunk of the European larch. The activity of agaricin is due to

agaricic, agaricinic, or agaric acid. The pure acid occurs as a white, silky powder made up of minute prismatic or lamellar crystals, and having a bitter taste. It is soluble in alcohol, and in hot water, and but slightly so in cold water, ether, and acetic acid. It forms soluble salts with the alkali metals. *Agaricic acid* is the preparation from agaric generally used in therapeutics under the name of agaricin. The commercial agaricin, on the other hand, is an impure resinous product obtained by extraction from the crude drug, and is much weaker in its effects than the acid.

DOSE.—The dose of *agaricic acid* is ⅟₁₅ to ½ grain (0.004 to 0.03 Gm.). It is usually given in pill form, but may also be administered hypodermically, when the dose should be one-half smaller. The *resinous agaricin* is sometimes used, the dose being from 1 to 5 grains (0.065 to 0.3 Gm.). The doses given should at first be small; they can then gradually be increased as the patient becomes partially tolerant to the effects of the drug.

PHYSIOLOGICAL ACTION.—Agaricic acid in therapeutic doses decreases markedly the activity of the sweat-glands. It probably acts on the secretory nerve-endings to these glands (Hofmeister), thus resembling atropine in its action. It exerts, however, no inhibiting influence on the other secretions of the body, including the salivary secretion, and does not affect the pupils. In larger doses it causes purging and sometimes vomiting by an irritating effect on the gastrointestinal tract. No serious constitutional results are ever produced by it when used internally because of the slowness with which it is absorbed. It has no cumulative action. Toxic effects from it may be observed, however, upon its intravenous injection in large doses into animals, and less readily upon subcutaneous injection. It excites primarily, and secondarily causes, progressive paralysis of the bulbar centers, including the vagal and vasomotor centers. The animal shows marked weakness, becomes dyspneic, has convulsions, and dies as a result of paralysis of the respiratory center. Subcutaneous injections of agaricic acid produce inflammation of the surrounding tissues, sometimes followed by abscess formation. When applied to abraded areas or to mucous membranes it acts as a local irritant.

Agaricin is a powerful poison for involuntary muscle, producing a marked and long continued rise of tone. It is suggested that this action affecting the muscular tissue surrounding the sweat glands prevents the secretion of the sweat, partly by more or less obstruction and by preventing peristaltic movements, and partly, perhaps, by limiting the blood supply. McCartney (Jour. Pharm. and Exper. Therap., July, 1917).

THERAPEUTICS.—Agaricin (agaricic acid) is of great value in the treatment of the **night-sweats** of pulmonary tuberculosis. Doses of ⅛ to ½ grain (0.01 to 0.03 Gm.) are generally effective; according to Conkling, ⅟₁₂ grain (0.005 Gm.) will often suffice. Where the gastric digestion is good, it is well tolerated, and often causes diminution or even complete disappearance of the sweats (Andral, Legougeux), especially in the second and third stages of the disease (Combemale). The action begins two hours or more after administration, and reaches its height three hours later. Taken before retiring, agaricin will sometimes prevent the occurrence of a night-sweat, thereby relieving the patient from the consequent exhaustion.

While not as certain a remedy as atropine, it is advantageous in not causing the other unpleasant effects of the latter, such as drying of the mouth and fauces, nausea, and dilated pupils. It may be given in combination with aromatic sulphuric acid, which has a similar action in reducing sweats. Where agaricin is found to cause gastrointestinal irritation and a tendency to diarrhea, it is sometimes prescribed with small amounts of some preparation of opium,—Dover's powder, for example.

Agaricin is used to counteract **excessive sweating** from other causes than phthisis, including various infections and intoxication by certain drugs (coal-tar antipyretics, salicylates). It has also been employed **to arrest the secretion of milk.** Its action can be kept up, if desired, by reducing the dose previously administered, and giving small doses repeatedly.   S.

AGGLUTINATION TEST.

—This test, also known as the **Widal reaction** or the **Gruber-Widal reaction,** is used to establish the presence of typhoid fever. It is based upon the fact that in this disease the specific bacteria in free dilution "agglutinate," that is to say, adhere to one another and lose their motile power, thus forming clumps or masses in the solution examined.

The essential feature of this test is that, while normal serum, *i.e.,* the serum of a normal individual, when diluted up to a certain limit, will agglutinate many bacteria besides the typhoid bacillus, the latter organism causes the production of so great a quantity of the substance "agglutinin," which provokes the phenomenon, that, even when a drop of serum from a typhoid patient is diluted 50 times or more with saline solution, agglutination of typhoid bacteria, obtained from a recent culture of these germs, will occur. The reaction is only reliable, in fact, when the degree of dilution is not below 1 to 50.

The *microscopic* reaction requires a slide with a concave depression in the middle of one of its surfaces. A small quantity of the patient's serum is obtained by pricking the ear or the finger. This quantity is diluted in fifty times its volume of saline solution. A drop of this is then placed on a cover-glass, with a drop or loopful of fresh bouillon of genuine typhoid bacilli. The cover-glass is then inverted and placed over the concavity of the slide in such a way as to cause the mixture to hang downward. Hence the term "hanging drop" method. The edges of the cover-glass being then sealed with paraffin or vaselin, the slide is examined under the microscope, using the one-twelfth oil-immersion lens, and the clamping and loss of motility of the typhoid bacilli ascertained. If more than 4 bacteria are permanently agglutinated, the test is positive.

This method is only applicable, however, in hospitals, where a clinical microscope is available, unless the physician carries his microscope to the patient's home. This inconvenience can be readily obviated, however, by dipping a piece of absorbent paper in the patient's blood. When dried this paper can be used for the test by placing it in forty to fifty times the quantity of saline solution that the paper contains of serum. The latter will then dissolve in the saline solution, and a drop of the mixture with the drop of typhoid bacilli culture can then be used as described above.

Or again, "3 drops of blood are taken from the well-washed aseptic finger-tip or lobe of the ear, and each lies by itself on a sterile slide, passed through a flame and cooled just before use; this slide may be wrapped in cotton and transported for examination at the laboratory. Here one drop is mixed with a large drop of sterile water to redissolve it. A drop from the summit of this is then mixed with 6 drops of fresh broth culture of the bacillus (not over twenty-four hours old) on a sterile slide. From this a small drop of mingled culture and blood is placed in the middle of a sterile cover-glass, and this is inverted over a sterile hollow ground slide and examined. A positive reaction is obtained when all the bacilli present gather in one or two masses or clumps and cease their rapid movement inside of twenty minutes" (Green-Hughes).

The test may also be carried out without the aid of a microscope; this is the *macroscopic reaction.* Several bouillon cultures being available, 5 c.c. of each culture are placed in as many test-tubes as there are cultures. To each test-tube is then added sufficient serum of the suspected case to obtain a solution of 1 to 50. The test-tubes are then kept at blood or room temperature from three to seven hours. Their contents will then have become clearer, the bacilli having been precipitated to the bottom of each test-tube if the reaction is positive. It is obvious, however, that the microscopic reaction is preferable and less liable to mislead.

That the value of the Widal reaction is very great is now generally recognized. Kneass and Stengel in statistics based on over 2000 cases give 95.2 per cent. as the proportion in which true cases of typhoid fever had given a positive reaction, while no reaction occurred in 98 per cent. of the cases which eventually did not prove to be typhoid. Abbott, in statistics based on 4154 cases for which the Widal reaction was taken in the municipal laboratories of

Philadelphia, places at only 2.8 per cent. the possibility of error. S.

A simplified agglutination test is recommended by the writer. By drawing the blood direct into distilled water the corpuscles are destroyed, and the clear fluid left can be used just as well as the serum alone. Two drops of blood are drawn into 1 c.c. of distilled water. One drop represents about 0.05 c.c. serum, and the dilution is about equivalent to 1 in 20. To the limpid red fluid 1 c.c. of saline is added, then dilute with saline sufficient to make up 1 c.c. each time. Control tests with the ordinary technic confirmed in every respect the reliability of this simplification of the Widal test. Liebermann (Deut. med. Woch., Dec. 10, 1914).

After an experience in 275 patients, the writers emphasize the need for repeated agglutinations at intervals in the case at least of persons previously inoculated. They do not think that any diagnostic inference can be drawn from a consideration of the titer in inoculated persons, in cases in which only one examination has been made, as individuals vary so diversely in their agglutinin response to infection or inoculation. Donaldson and Clark (Lancet, Sept. 23, 1916).

The agglutination test for typhoid, paratyphoid A, or paratyphoid B, infection has not lost its diagnostic value as the result of prophylactic inoculation against these infections. The only changes inoculation has produced are the need for the adoption of accurately quantitative agglutination tests, the use of a standardized agglutinable culture, and the need of repetition of the tests to determine the curve of agglutination. Walker (Lancet, Nov. 25, 1916).

The writer observed a multiple or para-agglutination of the saprophytic germs with various germs—those of the cholera vibrio, typhoid or paratyphoid, Flexner or Y dysentery bacilli in various combinations, etc. In 1 case, for example, there was agglutination for cholera at 1:50, for typhoid at 1:200, and for dysentery bacilli at 1:100, with marked agglutination of certain bacteria found which are not usually regarded as pathogenic. Baerthlein (Münch. med. Woch., Oct. 31, 1916).

The writer made intracardiac, and, in 2 cases, intravenous injections of an agglutinin so strong that it could be detected in minute quantities. He found that in general a foreign serum disappears more quickly from the blood of an animal sensitized to that serum than from that of a normal animal. It disappears more quickly from the blood of highly reacting animals than from that of slightly reacting animals. Hempl (Jour. of Immunology, Feb., 1917).

The following simple and rapid macroscopic method is suggested for the application of Moss's test: Using citrated Serum II and Serum III, made to contain 1.5 per cent. of sodium citrate to prevent coagulation of the blood to be added, and preserved with 0.25 per cent. tricresol, a glass slide is prepared by placing one or two drops of Serum 11 on its left end and an equal amount of III on the right end, then two small drops of the blood to be tested are secured from a finger prick and mixed with the two serums. A positive agglutination is shown by clumping of the red cells which occurs within less than a minute and which is easily seen by the naked eye. The group number of the corpuscles is readily determined from the combination of reactions in the two tests by comparing the slide with the two middle columns of the following table.

RELATION OF THE FOUR BLOOD GROUPS.

Corpuscles

Group:	I	II	III	IV	
I	o	+	+	+	I
II	o	o	+	+	II
III	o	+	o	+	III
IV	o	o	o	o	IV
	I	II	III	IV	

Beth Vincent (Jour. Amer. Med. Assoc., Apr. 27, 1918).

Active convection currents in tubes increase the rapidity of agglutination materially, especially in bacterial suspensions which agglutinate rather poorly. Convection currents are best secured by immersion of the agglutination tubes in the waterbath at 55° C. until the water rises to only ⅛ to ¼ the height of the column of fluid tested. This technique gives uniform results and materially shortens the time of incubation. Topley and Platts (Lancet, June 8, 1918).

S.

AGORAPHOBIA.—This term is applied to a variety of obsessions in which fear of not being able to cross an open space, a room, street, square, etc., predominates. The patient carries out the act, however, when compelled to do so, or in company. He may be quite normal otherwise, though condemned to a sedentary life. It is often associated with acute neurasthenia, and occasionally with the chronic form of this disease.

AGURIN, a diuretic, is a double salt of theobromine sodium and sodium acetate, which contains 60 per cent. of theobromine. It occurs in the form of a fine crystalline powder, which is freely soluble in water, and but slightly so in cold alcohol.

MODES OF ADMINISTRATION.—Agurin is hydroscopic and, in aqueous solution, readily splits into its components. Hence, the advisability of prescribing it in capsules or in tablets, 5-grain tablets being available in the shops. The dose is from 5 to 10 grains (0.3 to 0.6 Gm.) three to five times a day. It is also absorbed from the rectum when given in an enema of plain water.

THERAPEUTICS.—Agurin is especially efficacious as a diuretic in cardiac dropsy and acts well in combination with digitalis. It acts like theobromine (*q.v.*) and is, unlike diuretin, well borne by the stomach. It also gives good results in **interstitial nephritis,** especially when combined with the milk diet. This applies also to **hepatic cirrhosis,** though to a less marked degree. Agurin presents the advantage of promoting diuresis without increasing the blood-pressure, a property which renders it particularly useful in cases of **dropsy of cardiac, renal, or hepatic origin** in which arteriosclerosis renders diuretics which raise the blood-pressure dangerous.

S.

AINHUM.—African word meaning "to saw off."

DEFINITION.—Ainhum is a disease occurring exclusively in negroes and consisting in the spontaneous amputation of the little toe by an adventitious fibrous band.

SYMPTOMS.—The first indication of the disease is a furrow on the lower surface of the little toe, and occasionally other toes, at the proximal interphalangeal joint. This furrow, the result of the circumferential pressure exerted by a fibrous ring, gradually deepens until the bone is reached, this process taking several years, sometimes as many as ten. The distal portion of the toe becomes greatly hypertrophied, then finally drops off, the stump healing without further complications in the great majority of cases. It does not give rise to much suffering, owing to its very gradual progress. It is sometimes mistaken for leprosy. It has been observed in the white race also.

Though rare in the United States, ainhum is so common in India that Crawford found a case in every two thousand surgical patients in Indian hospitals. The absence of pain or inconvenience in many cases also probably prevents their being reported. The ultimate result of the disease, which begins as a crack or fissure, is the spontaneous amputation of one or more fingers or toes by a gradual circular strangulation. In the writer's case, complete amputation of one toe and partial amputation of another had occurred before the patient sought medical assistance or appreciated his condition. It is rare in females, and is almost exclusively confined to the dark-skinned races, only 4 cases having been reported in whites. It is probably a trophoneurosis of unknown origin. N. D. Brayton (Jour. Amer. Med. Assoc., July 8, 1905).

Case of ainhum in a white girl in Florida. The case is of interest because of the appearance of ainhum in the Southern States and heretofore reported in the negro race only. When ulceration takes place the ulcer assumes a resemblance of a necrotic ulcer with a distinct nauseous color. As advanced by Unna, the condition is a sclerodermic callosity, with ring formation, producing a stagnating necrosis. The tumefaction indicates a stagnation, resulting in degeneration, retraction, and finally disappearance of the phalanges. The disease sometimes covers a period of several years. Eskridge (Med. Rec., Sept. 17, 1910).

Two cases of ainhum that the writer has cared for at Garfield Hospital Dispensary. He watched the progress of the case for two years, and showed photographs and skiagraphs of them, taken at the beginning and end of observation. One case, in a negress, a native of Maryland, was of sixteen years' duration, but only slightly advanced. The pain in the crack was, however, sufficient to induce her to have the toe amputated. The specimen showed the groove in the soft tissues and the slight atrophy of bone.

The other case, also in a negress, a native of Georgia who had lived fifteen years in the District of Columbia, was of about twenty-five years' duration and much more marked than the other case; the groove around the toe was deepest on the plantar and inner margins of the toe and had penetrated almost to the toe-nail. The middle phalanx was practically gone; only the nail-bearing part of the ungual phalanx remained; the basal phalanx was atrophied about one-half. The advance of absorption of bone was quite plain in the skiagraphs. The skin of the feet and hands showed a scaly condition. As the toe had given but little pain, the patient declined to have it amputated, and had therefore come for treatment. Truman Abbe (Washington Med. Annals, Nov., 1910).

ETIOLOGY.—Ainhum is always observed in negroes, especially of the western coasts of Africa and South America. A number of cases have also been reported in the United States by Bringier. Hindoos are said to also suffer from the disease. Self-mutilation has been suggested by some observers, but the likelihood of this cause is very slight. Heredity does not seem to play any rôle in its production.

PATHOLOGY.—The lesions observed have been hypertrophic thickening and retraction of the derma, with consequent atrophy of the underlying bone (Hermann, Weber, Wucherer, Schüppel). It has been confounded with congenital amputation, but, as stated, ainhum is never congenital. That the disease bears some connection with leprosy is insisted upon by some authorities. According to Zambaco, Pacha, undoubted symptoms of leprosy are present in all cases of true ainhum. It should be looked upon as an attenuated form of the latter disease. Its relations to scieroderma are explained by the fact that this latter affection is a special form of leprosy. It has also been attributed to syphilis, larvæ, and atavism.

The writer agrees with Matas in terming ainhum a trophoneurosis. Personal case in a negress of 65 years whose right little toe was affected in the characteristic way. The toe was disarticulated at the metatarsophalangeal joint under cocaine anesthesia, and the cicatrix has since remained in healthy condition. H. N. Blum (Med. Record, Oct. 22, 1904).

No definite and undisputed cause for the lesion has yet been proved, but the writer thinks that there is most to be said in favor of de Silva Lima's view that it is due to traumatism. The splay-footed negro is especially liable to such, and the groove around the toe in this disease, both macroscopically and histologically, is a cicatrix. The later fatty and atrophic conditions in the amputated toe are not yet fully explained, but may depend on local cicatricial formations or may be of trophic origin. Wellman (Jour. Amer. Med. Assoc., March 3, 1906).

TREATMENT.—Surgical measures alone prove of value in these cases. Early **section** of the fibrous ring is sometimes sufficient to arrest the progress of the disease, or **division of the skin** down to the periosteum on the opposite side of the seat of the disease may be resorted to.

Murray successfully treated a case by dividing the skin and all the tissues down to the periosteum, on the side opposite to the seat of the disease.   S.

AIROL, or bismuth oxyiodogallate $[C_6H_2(OH)_3.COO.BiIOH]$, is a compound of gallic acid and bismuth subiodide. It occurs in the form of a bulky, grayish-green powder, devoid of odor or taste. It is insoluble in water, alcohol, chloroform, and ether, but is slightly soluble in glycerin and is dissolved in alkaline solutions and dilute mineral acids. When exposed to moisture, including wound secretions, it is gradually changed into a reddish powder, due to the liberation of a portion of its iodine: this change occurs with great rapidity when boiling water is applied to airol.

MODES OF ADMINISTRATION.— Internally airol has sometimes been given in doses of 2 to 5 grains (0.13 to 0.32 Gm.). Externally it is used principally in the powder form, which is dusted over the surface involved after it has been washed with hydrogen peroxide or other cleansing agent. It may also be applied in an ointment containing about 2 to 4 drams of airol to the ounce of petrolatum, or in a 10 per cent. glycerin emulsion containing equal parts of glycerin and water. The latter preparation may be injected in septic areas. In the treatment of skin lesions it has been applied as a paste containing 2 parts each of glycerin and mucilage to 1 part of airol, mixed with a sufficient amount of refined clay or kaolin (Brun's paste). Airol has also been used as a vaginal suppository. An airolated gauze (20 per cent.), similar to iodoform gauze, is frequently employed. The fact that this substance is decomposed by free contact with water should always be kept in mind.

PHYSIOLOGICAL ACTION.—When used internally or by injection in large amounts, airol has been known to cause symptoms similar to those of bismuth poisoning. Thus Semmer witnessed a case in which 55 grains of airol as a 10 per cent. solution in olive oil injected into an abscess resulted within three days in softening of the gums, darkening of the buccal mucous membrane, foul breath, headache, nausea, and prostration. Marked irritative effects have also been observed (Zelemsky, Goldfarb), though a total amount of 15 grains taken within three days was found by Haegler to cause no unpleasant effects.

THERAPEUTICS.—Airol is valuable externally as an **antiseptic,** astringent, desiccant, and protective. Its germicidal properties are mainly due to the liberation of iodine upon exposure to moisture.

Haegler considers airol the equal of iodoform in disinfecting power, and it has the added advantage of being without odor. It is frequently used as an antiseptic dressing for open wounds, including **surgical wounds,** and generally causes no pain when applied. It has been applied to **infected ulcers** of different kinds, **varicose ulcers** (Fahm), **burns** of the second degree, and to the lesions of various skin diseases, such as **intertrigo** (de Sanctis), etc. It has proven useful when injected with glycerin in **abscesses** of pyogenic or primarily tuberculous origin.

In **ulcerations of the cornea,** airol has been applied in powder form with success (Gallemaerts, Bonivento).

Airol has been used for the treatment of **uterine** and **vaginal inflammations.** It may be incorporated in the usual cocoa-butter suppositories for vaginal use, or introduced into the uterus and vagina on gauze moistened with a liquid mixture. Delbert dips a wick of aseptic gauze in a 1 to 4 emulsion of airol in glycerin and inserts it through the previously dilated cervix into the uterine cavity; he then packs the vagina with tampons of absorbent cotton dipped in a 1 to 20 emulsion, and does not remove it for forty-eight hours (Manquat).

Airol may be given where an astringent effect on the intestinal tract is desired. Fahm has recommended its use in **tuberculous enteritis.**   S.

ALBARGIN, or gelatose silver, an antiseptic and germicide, is a compound of silver nitrate 15 parts and gelatose 85 parts. It occurs as a light, brownish-yellow, shining powder, which is freely solu-

ble in equal parts of both cold and hot water, making a permanent solution if not exposed to light. It is incompatible with ferric and ferrous chlorides, tannin, opium, resins, and the essential oils.

THERAPEUTICS.—Albargin is mainly used as a substitute for silver nitrate in the treatment of **gonorrhea.** Its aqueous solutions being neutral, it may be used as injections in strengths from $\frac{1}{2}$ to 2 per cent. Its molecule being smaller than that of albuminous preparations of silver, it is thought to penetrate more thoroughly and promptly the diseased tissue and destroy the gonococci therein. Albargin has also been found efficacious in the treatment of **chancroids.** Its use is painless, and it does not irritate mucous membranes; it may safely be used, therefore, in the treatment of **gonorrheal ophthalmia.**   S.

ALBUMINURIA.— D E F I N I -
TION.—The presence of albumin in the urine, a condition now known to occur under many circumstances without necessarily indicating the presence of serious morbid changes in the kidney.

Albuminuria may be *true*—when the albumin is dissolved in the urine—or *spurious,* when caused by admixture of semen, pus, or blood in the urine. Spurious albuminuria is easily distinguished from the true form by the aid of the microscope. Both kinds of albuminuria may occur simultaneously.

Domenico Cotugno discovered, in 1770, that urine may contain albumin; by boiling a sample of urine he found that pure albumin was precipitated. It was long maintained by all authors that albuminuria was always a symptom of disease, but of late many authorities have admitted that albuminuria may be compatible with perfect health.

Posner maintains that albumin is always found in the urine, but normally in too small quantity to be revealed by the ordinary reagents. To demonstrate the presence of albumin in normal urine Posner evaporated large quantities of urine at low temperature and tried the different reagents in the concentrated urine. His experiences were repeated and his views supported by Senator and by Leube, who, however, did not find albumin in all cases. Von Noorden, Winternitz, Lecorché, Talamon, and other authors do not admit that albumin is a constituent of the normal urine; but this was recently denied by Mörner, who found that it invariably contained at least 22.78 mg. (about 3.5 of a minim) per liter.

Different kinds of albumin may be present in the urine; generally the proteids contained in the blood-serum are to be found,—viz.: (1) the serum-albumin, and (2) the globulin, or paraglobulin; in most cases both these proteids are present, but in varying proportions. In some cases there may also be found (3) hemialbumose, or propeptone, a mixture of different albumoses which are not precipitated by boiling; (4) nucleoalbumin, which has also erroneously been called "mucin," and (5) peptone. Joachim found pseudoglobulin in every case of albuminuria, while euglobulin was often absent. The albumin content mostly exceeds that of the globulin.

The urine may, of course, also contain albumin in connection with hematuria and hemoglobinuria, but such cases cannot be classed as true albuminuria.

PHYSIOLOGICAL ALBUMINURIA.—Regarding the origin of the albumin in the urine only guesses can be made; two theories are possible: (1) the albumin may come from

the glomeruli; (2) from the tubular epithelial cells.

Formerly the opinion predominated that the fluid which escaped from the glomeruli was albuminous, but that the albumin was absorbed during the passage through the healthy renal tubules, diseased tubular epithelium being unable to absorb the albumin. This has not been proved, however, and most modern authors believe that albumin is not contained in the urine coming from the glomeruli, except when these are diseased or when the pressure of blood in the glomeruli is abnormally great. Runeberg, on the contrary, is of the opinion that albuminuria is caused by low pressure of blood, and supports this opinion by experiments with animal membranes, but experiences with dead membranes cannot be regarded as conclusive for the action of the living kidney.

Von Noorden and other authors regard the tubular epithelium as the unique source of albuminuria. These epithelial cells are subject to successive disintegration: when this is minimal, and successive traces, only, of albumin are found in the urine, the albuminuria is physiological; when the disintegration of the tubular epithelial cells is augmented and hastened by disease, a morbid albuminuria takes place. In his opinion, this theory is supported by the fact that nucleoalbumin, of which the protoplasm of the cells undoubtedly is the source, is always found in normal urine.

Benign albuminuria depends, according to the writer, on a vagatonia which is itself due to a reduced tonus of the sympathetic caused by aplasia and insufficiency of the chromaffin system. In vagatonia the renal vessels are constantly dilated because of the decreased tone of the sympa-

thetic. When, in a person so affected, a greater quantity of adrenalin is secreted because of any reason whatever, the reduction of tone of the sympathetic becomes still greater, and consequently the dilatation of the renal vessels becomes so great as to give rise to renal stasis and so to an albuminuria. C. v. Dziembowski (Berl. klin. Woch.; Corresp. blatt f. schweizer Aerzte, Jan. 19, 1918).

Senator considers physiological albuminuria in the same light as physiological glycosuria, and, among the causes that give rise to it in susceptible individuals, he mentions: severe exertion of the lower extremities, eating and digestion of hearty meals, menstruation, cold baths, psychical excitement, etc. He deems albuminuria pathological only when it does not disappear promptly on the cessation of the particular stimulus that caused it. Physiological and allied forms of albuminuria are attributed to congenital predisposition of the individual to disease of any organ which directly or indirectly may influence the elimination of albumin.

The influence of exertion was shown on 528 soldiers by the writers. Of these 56, or 10.6 per cent., had albuminuria. The amount of albumin was small in the great majority. To determine the influence of work and rest on the excretion of urine, the latter was examined immediately after work, and in the morning after a night's rest. It was found to be present in 11.5 per cent. after working, in 7.9 per cent. after rest. M. Laber and P. Lauener (Corresp. Bl. f. schweizer Aerzte, July 24, 1915).

In soldiers the writers found complications in the kidneys directly after acute infectious diseases in 17 per cent. of the men examined, irrespective of whether the men had been serving at the front or had never reached the trench line. In 6 of 18 men the albuminuria had developed

after acute tonsillitis. There was a history of some old acute infectious disease in 40 per cent. of the eighty men from the front and in 50 per cent. of the thirty others. In 22 per cent. there was primary nephritis occurring in previously healthy men. In two of the men the albuminuria developed after antityphoid vaccination. Chronic albuminuria which may be well borne in civilian life is extremely liable to give trouble under the stress of military life. Merklen (Annales de Méd., May-June, 1918).

From a pathological point of view the causes of albuminuria may be divided into three groups: 1. Disturbances of circulation. 2. Changes of the tubular epithelial cells or of the walls of the blood-vessels of the kidney. 3. Changes in the composition of the blood.

1. All disorders of circulation capable of causing a venous renal congestion will increase the blood-pressure in the capillaries of the kidney, and thus give rise to a transudation of albuminous liquid; when the congestion is very great the urinary tubules may even be compressed and the escape of the urine rendered difficult. When this is the case and when, also, the supply of arterial blood is diminished, the tubular epithelium will be damaged, and the first result of all this is albuminuria. It is very improbable that arterial congestion ever produces albuminuria, although the experiments of Munk and Senator tend to prove the contrary. Leube found in the early stages of aortic insufficiency, not accompanied by cyanosis, edema, etc., a slight albuminuria. Pathological examination of the kidneys showed the walls of arteries and capillaries much thickened. He makes these changes and their consequences responsible for the maltnutrition of the kidney and its result: albuminuria.

2. Changes of the tubular epithelia and the walls of blood-vessels of the kidneys may, as already stated, be due to disorders of circulation, but they may also be caused by different poisons and toxins. When albuminuria is chiefly caused by degeneration of the tubular epithelia, their protoplasm dissolves in the urine, and nucleoalbumin in great quantity is contained in it, combined with serum-albumin and globulin.

Menge and Schreiber noted albuminuria in several cases in which the kidney had been palpated bimanually, as a result of the circulatory changes produced during the examination. This procedure has been used by Schreiber in the diagnosis of doubtful cases of floating kidney.

3. When the composition of the blood is altered, the urine often becomes albuminous. This can be proved experimentally by injecting egg-albumin, soluble casein, hemoglobin, etc., into the veins of animals; the quantity of albumin excreted after the injection will generally exceed the quantity injected. Similar results may be obtained by the injection of peptone and propeptone, whereas the albuminates are generally inoffensive. Ingestion of a very large quantity of egg-albumin is liable to provoke albuminuria.

Semmola has tried to prove that albuminuria is always caused by changes of the blood characterized by abnormal diffusibility of its proteids, and, in his opinion, the pathological changes in the kidneys are consecutive to the albuminuria. Though his theory is not generally accepted, Rosenbach has adopted it for the albuminuria which is not caused by nephritis, and regards it in such cases as a salutary and regulating process, if such can occur at all.

In most clinical cases different causes

are simultaneously active, and it is generally very difficult to determine which is the preponderating etiological factor. L. Williams ascribes the majority of cases of albuminuria either to altered blood states or to failure in the normal vasomotor mechanism.

> The majority of the cases are due to either altered blood states or to failure in the normal vasomotor mechanism. This failure may manifest itself in one or two directions. In the first, chiefly by some means so far undiscovered, the blood-pressure in the splanchnic area arises and is maintained at a sufficiently high level to induce a renal plethora and consequent albuminuria. Of such are the cases of hyperpiesis, as in the instance quoted. In the second place, owing to a local or general vasodilatation, the blood-pressure in the splanchnic area falls to the point at which a renal stasis is induced. Of such are the cases of cyclical, postural, and athletic albuminuria, of which also instances are cited, cases which, for the most part, occur in young adults in whom the vasomotor response is either undeveloped or for some reason is inadequate. Having regard to these facts, the writer ventures once more to insist not only that, of itself, albuminuria affords no evidence of renal disease, but that, of itself, it does not present even a reasonable suspicion of the existence of such disease any more than, of itself, dyspnea presents a reasonable suspicion of cardiac disease. L. Williams (Clin. Jour., Apr., 1908).

It is, nevertheless, true that traces of albumin, and even a rather considerable amount of it, may be found in the urine of persons otherwise healthy and presenting no symptoms of disease of the kidneys or of the organs of circulation.

Many clinicians, therefore, admit that albuminuria may be regarded, in some cases, as physiological; this is, however, contested by many.

> Case in which for over twenty years the patient had been passing large quantities of albumin in the urine, 3 grams per liter. Microscopic examination revealed no casts or corpuscles, and there was nothing to suggest renal trouble. The heart was normal in size, the sounds were normal, blood-pressure was in the limits of the normal, and there was little or no arterial thickening. The patient has maintained his usual high standard of health, and, although he had always been thin and spare, he is very tough. The most remarkable feature of the case, however, is that all the members of the patient's family exhibit the same peculiarity. They are all perfectly well, and, considering the age the parents have attained (87 and 78 respectively), such a case as this should have an important bearing on the question of rejection or "loading" of candidates for life insurance. Fergusson (Brit. Med. Jour., Mar. 19, 1910).

Virchow described a physiological albuminuria in infants, occurring in the first days of life, and explained it by the sudden changes of circulation taking place immediately after delivery.

Flensburg and Sjöquist have shown that albuminuria regularly occurs in the first days of life, and that the urine also contains an extraordinary quantity of uric acid crystals; probably the albuminuria is then due to the irritation of the kidneys caused by these crystals. Ebstein and Nicolaier have shown experimentally that when the kidneys are forced to excrete a surplus of uric acid which cannot be dissolved, but goes to the bottom in the form of crystals, the urine commonly contains albumin and sometimes even blood.

Gull found a certain form of physiological albuminuria in adolescents about the age of puberty, especially in weak and pale individuals. Other authors, among whom is Quain, have

noticed that this condition is quite frequently associated with masturbation.

Lommel found that 19 per cent. of young men (14 to 18 years old) suffered from albuminuria without having nephritis. The albuminuria had an intermittent character and was orthostatic in type.

Dunhall and Patterson and Collier found albuminuria (0.2 to 15 per cent.) after severe exercise (such as rowing and running in races) also in healthy subjects.

> Albuminuria is of fairly constant occurrence in patients who have acute or chronic suppuration. If an abscess is deep and under considerable pressure, albuminuria is more likely to occur. If the abscess is drained, the albuminuria disappears. Marcozzi (Folio Urologica, Feb., 1914).
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> The writer had several cases that showed a transient albuminuria after lavage of the stomach, although nothing of the sort was present before. Schiff (Wiener klin. Woch., May 28, 1914).
>
> The writer examined the urine of every soldier admitted to the surgical hospital in his charge, a total of 3210 men. Albumin was found in 13 per cent. but never in large proportions. Engel (Deut. med. Woch., Nov. 23, 1916).

PHYSIOLOGICAL CYCLICAL, ORTHOSTATIC, AND ORTHOTIC ALBUMINURIA.

The question of physiological albuminuria in adults has been much discussed during the past few years and has particularly engaged the interest of the medical men employed in insurance work.

> Stirling was the first to call attention to intermittent albuminuria in children in connection with the position of the body, and he styled it *"postural albuminuria."* The writer holds that this is the best name for

it, as neither the orthostatic nor the lordotic attitude ever induce it except in the predisposed. Of the 204 children examined, albuminuria could be induced by lordosis alone in only 3 per cent., and by a change from the seated to the erect posture (orthostatism) only in 1.3 per cent. Both together, the children not keeping still, induced albuminuria only in 1.6 per cent. The findings in the various groups listed show that the restlessness of children responds to a physiologic demand, and that children should not be expected to sit still in school. The school desk should be arranged. Jeanneret (Arch de Med. des Enfants, Sept., 1915).

A study of 5 cases of orthostatic albuminuria led to the conclusion that it is a general systemic disturbance, manifesting itself in faulty development, as shown by a general visceroptosis, a "drop heart," a generalized muscular and visceral atonia, which is known to be associated with varying degrees of vasomotor instability. The symptoms so commonly complained of, such as headache, lassitude, constipation and loss of weight, are the natural results of physical conditions. The increased lordosis that is usually present is regarded as a symptom due to the faulty muscular development and tone of the lumbar muscles. The low pulse-pressure is undoubtedly the cause of the albuminuria rather than a mechanical interference with the venous return from the kidneys. Mason and Erickson (Amer. Jour. Med. Sci., Nov., 1918).

It is characteristic of physiological albuminuria that the quantity of albumin is generally small and that the excretion is, in most cases, intermittent, or cyclical. Leube, Pavy, Fürbringer, Klemperer, and many other authors have studied this condition.

Pavy introduced the denomination "cyclical albuminuria" for the cases in which the albuminuria ceases and returns at regular intervals.

Stirling ascribes cyclical albuminuria to a sudden shock from the blood-pressure upon assuming the upright position on arising, but Rudolph showed that albumin also appeared in the urine when the upright position was assumed very slowly.

Pavy likewise insists upon posture as the invariable cause of cyclical, or intermittent, albuminuria, the excretion ceasing when the subject is in the recumbent position and going on only when he is walking or standing. The cycles are commonly completed within the day, but in a case narrated by Klemperer there were two cycles, the maximum of albuminuria taking place in the forenoon and afternoon.

Hauser concludes that these cases can always be traced back to an uncured nephritis or to some acute infection (notably scarlatina), and puts no credence in a functional disorder. In other words, he always considers cyclical albuminuria as the expression of some pathological factor.

Oswald attributes all forms of albuminuria of adolescence to irritation of the renal epithelium.

Moritz ascribes cyclical albuminuria to some insufficiency of the circulatory apparatus, having observed that the increased blood-pressure which normally occurs after moderate exercise is followed by abnormally low pressure in individuals that are subject to cyclical albuminuria.

The diagnosis of physiological albuminuria ought not to be made except in cases when persons presenting no other symptoms of disease excrete, constantly or intermittently, a urine containing a scanty quantity of albumin, but no morphotic elements and especially no casts. The centrifugal apparatus, now in general use, will certainly contribute to restrain the number of these cases. The urine should be obtained by catheterism in all doubtful cases.

The prognosis is generally considered good (Broadbent, Beck, Dukes, Tiessier, Posner). Nevertheless it is still justifiable for life-insurance examiners to be cautious in accepting persons suffering from albuminuria.

It is no longer justifiable for life insurance and other such examiners to take the serious view hitherto accepted by most clinicians of physiological albuminuria. When it is found that the excretory function is being properly performed; that the substances normally gotten rid of through the kidneys are not being retained in the organism, and that the albumin in the urine may be diminished by lessening the hydrostatic pressure upon the renal capillaries by increasing the coagulability of the blood, there is every reason to conclude that the kidneys are free from organic disease, that life is not in the least endangered. Instances reported in which excellent results have been achieved by the administration of calcium chloride in doses of 20 grains three times a day. Calcium lactate in the same dosage is also useful. Both increase the coagulability of the blood. A. E. Wright and G. W. Ross (Lancet, Oct. 21, 1905).

Very small proportions of albumin should not be taken into account in relation to life insurance, and consequently the writer does not regard as of much moment the efforts to produce more and more delicate tests for albuminuria. The so-called physiological slight albuminuria after excessive exertion, sports, etc., may also be disregarded. The majority of cases of orthostatic albuminuria are also comparatively harmless; it is exceptional for nephritis to develop later in these cases. In examining it is important to note the absence of the higher blood-pressure characteristic of contracted kidney; also that

the urine is free from albumin during reclining. Fürbringer (Deut. med. Woch., Nov. 25, 1909).

Teissier distinguishes three groups of orthostatic albuminuria: The *true orthostatic albuminuria,* where the albumin appears very soon after assuming the erect posture. It disappears in the recumbent posture. The *mixed orthostatic albuminuria,* which, more slow in its development (usually not before ten and twelve in the morning), is found in persons with an earlier acute infection and believed to be due to actual organic changes in the kidney. The *associated orthostatic albuminuria* is also slower in making its appearance after assuming the erect posture and is associated with abnormal conditions of other organs (dilated stomach, enteroptosis, movable kidney, etc.).

Orthostatic albuminuria was noted by the writer in 14.9 per cent. of 1076 school children in Christiana. It was much commoner among the girls than among the boys, the figures being 13.3 per cent. and 3.5 per cent,. respectively. Bugge (Norsk. Mag. f. Laegevid., lxxiv, No. 12, 1913).

In a study of orthostatic albuminuria among 189 healthy English school boys, the writer found that 7.5 per cent. showed albumin on arising, 7 per cent. after breakfast, 10.7 per cent. after football, and 18 per cent. after a three-mile run. Nicholson (Pract., xciii, p. 113, 1914).

Analysis of 14 cases of orthostatic albuminuria, 9 being children at about puberty, 4 young men and 1 woman of 33. The writer concludes that it requires no special treatment, but differentiation is extremely important as otherwise unnecessary restrictions and other measures are imposed for the assumed underlying nephritis. This is particularly disastrous in these cases because persons with orthostatic albuminuria are usually frail and may be predisposed to tuberculosis; there is also a tendency

to oxaluria. The orthostatic albuminuria disappeared completely or became much attenuated when the oxaluria was arrested by giving a level teaspoonful of **calcined magnesia** two or three times a day. With nephritis, the albumin content of the urine shows little change day or night. Scheel (Ugesk. f. Laeger, Mar. 7, 1918).

The writer conducted an examination of the urine of 401 boys and 311 girls in the school before and after the gymnastics class and, when albuminuria was found, the child was ordered to bring morning urine for examination. The children were all of the upper grades in the school. Albuminuria before the gymnastics was evident in 8 per cent. of the boys and 24 per cent. of the girls; after gymnastics, in 14 per cent. of the boys and 33 per cent. of the girls. In both categories the percentages grew higher the older the children; among the girls of the sixth grade and higher grades the proportion was 49 per cent. Fully 90 per cent. were frail children among those with lordotic albuminuria, and 70 per cent. of those with albuminuria in general; only 10 per cent. of the total were lively healthy children. Hamelberg (Nederl. Tijdsch. v. Geneesk., Mar. 9, 1918).

Even when no casts can be found, albuminuria ought never be regarded as absolutely inoffensive. Although a cyclical albuminuria continuing years may be compatible with perfect health, many authors (Johnson, Greenfield, Bull, etc.) are of the opinion that it signifies the first stage of the evolution of granular atrophy of the kidneys. On the other hand, casts may be found in normal urine and do not mean nephritis. Tuttle, for example, believes that nephritis may exist without albuminuria.

The writer examined *post mortem* the kidneys of a youth of 16 who had had typical orthostatic albuminuria during the last 5 or 6 years, but who had been otherwise in normal health

until he contracted "galloping tuberculosis" of the lungs. Not a trace of inflammation could be discovered in the kidneys. He reports also 10 clinical cases in which orthostatic albuminuria was a chronic condition, but in which no tubular casts were ever found. On the whole, while albuminuria may coincide with tuberculosis, orthostatic albuminuria cannot be deemed an indication of this condition. Holst (Norsk. Mag. f. Laegevid., Nov., 1915).

The albuminuria often found in parturient women (Aufrecht saw it in 56 per cent. of all cases) must be regarded as physiological.

Albuminuria occurring during labor is a reasonable accompaniment of parturition; the quantity is greater than can be considered normal, and is often the greatest seen in any except a permanent pathological condition. The condition requires no especial and separate treatment, and cannot be considered a permanent pathological lesion. The albuminuria of labor is differentiated from the other by the presence of labor and by the fact that it ceases after parturition. The more abundant the albumin, the more gradual is its disappearance. The albuminuria of the puerperal period is the continuation of that of labor, and is never a separate condition. The albuminuria of labor is most pronounced toward the end of parturition, especially in cases of difficult or complicated labor. Circumstances which do not tend to make parturition especially difficult have no influence upon its albuminuria. The sediment of urine taken during labor shows organized material, including cylindroids, so often seen in cases of abundant albuminuria. These cylindroids are not abundant, and are to be distinguished from others by the fact that they contain superficial kidney epithelium in abundance, but not the elements which come from the deeper kidney structures. Jageroos (Archiv f. Gyn., Bd. xci, Hft. 1, 1910; Amer. Jour. Med. Sci., Nov., 1910).

In an exhaustive study of several patients the writers noted that the condition appeared in the strong and well-developed as well as in the weak and anemic types. They are inclined to believe that the explanation is to be found in a mechanical cause, resulting in congestion of the renal vessels, together with a local and general predisposition. **Supporting apparatus** by improving the posture, gave good results. Fischl and Popper (Boston Med. and Surg. Jour., May 4, 1916).

PATHOLOGICAL ALBUMINURIA. — Pathological albuminuria is found in pathological changes of the blood—as anemia, leukemia, pseudoleukemia, scurvy, icterus, and diabetes —even when the kidneys do not present pathological changes.

It is also found in many disorders of the nervous system, as epilepsy, migraine, psychosis apoplexy, neurasthenia, and Basedow's disease, etc. Delirium tremens has also been mentioned as a nervous disease often complicated with albuminuria. H. H. Schroeder regards excessive eating, overindulgence in alcoholic drinks and possibly tobacco as the most frequent causes of albuminuria.

Although the kidneys are theoretically believed to be healthy in the diseases mentioned above, there is no doubt that albuminuria, in many cases of this class, is caused by pathological changes of the kidneys.

In all febrile and especially in all infectious diseases albuminuria is a very frequent symptom. It has been noticed in enteric fever, diphtheria, variola, after vaccination, in erysipelas, influenza, rheumatic fever, pneumonia, etc. In these cases the albuminuria is caused by changes in the composition of the blood, increase of blood-pressure, rise of temperature, and finally by changes

in the structure of the kidneys, especially of the tubular epithelial cells caused by the toxic substances excreted.

The presence of albuminuria in pregnancy, as stated above, is common (56 per cent.). Casts are only found in about 50 per cent. of these cases of simple albuminuria. The so-called kidney of pregnancy is to be regarded as a specific toxic nephritis which tends to recur in subsequent pregnancies. The prognosis of it, if properly treated, is good.

Albuminuria has been observed in diseases of the intestines, dilatation of the stomach, ileus, ruptures, etc., and in renal venous congestion caused commonly by disease of the heart or the great vessels.

It is present in all diseases of the kidneys. Acute, as well as chronic, albuminuria is generally found in the diffuse forms of nephritis, as well as in circumscribed renal diseases—such as infarcts, abscesses, or tumors. After retention of urine the portion of urine first passed is frequently albuminous.

Albumin is found in many diseases of the ureter, the bladder, the prostate and urethra. Ballinger speaks of prostatic albuminuria as a name for an albuminous secretion from an hyperemic or inflamed prostate. This prostatorrhea is constant in chronic prostatitis and often increases regularly every ten to thirty days. It should not be taken for a true albuminuria.

> The writer recognizes the existence of a distinct and well-characterized form of albuminuria of rather favorable prognosis that is not due to a nephritis of toxic or infectious origin, to circulatory disturbances in the kidneys, nor to general cardiorenal disease, but to perversion of the gastro-intestinal and hepatic ductions. Croftan (Arch. of Diagnosis, Oct., 1908).

> After a study of 62 cases the writer challenges the prevailing view that while the diseased kidney may not permit urea, salt or even water to pass, it will allow the big albumin molecule to filter through. His study and experiments showed that inflamed kidney epithelium does not allow the passage of serum albumin, and that the albumin found in the urine does not come from the blood but must be secreted by the renal epithelium itself, an active, vital function. All the tests showed that filtering ascites fluid, pleural effusions, blood serum and similar fluids through a delicate animal membrane, such as the rabbit and cat intestine, the albumin content of the filtrate was about the same as that of the original fluid, and the proportion of albumin to globulin persisted unmodified, but when the membrane was hardened or otherwise rendered less permeable, the globulin was arrested first; with increasing impermeability none of the albumin passed into the filtrate or dialysate. Applying these findings to conditions in the kidney, either the proportion of globulin and albumin should be the same in the urine as in the blood, or the albumin should predominate. But this is not the case with diseased kidneys. A relative excess of globulin was found in the urine in simply congested kidneys and in orthostatic albuminuria. Mandelbaum (Deut. Archiv f. klin. Med., Oct. 24, 1920).

Merk found that many affections of the skin, eczema, pruritus, urticaria, erythema, and furunculosis, are intimately associated with albuminuria. Gunsberger noted albuminuria during a severe attack of acute urticaria. Nicolas and Jambon and Boas hold that albuminuria is a frequent accompaniment of scabies, but it is not satsfactorily settled how it produces this phenomenon.

Lancereaux observed frequently al-

buminuria in his cases of gouty, herpetic diabetes, but never noted it in his 40 cases of pancreatic diabetes. Glycosuria alone does not entail albuminuria. When it occurs it may be connected with arteriosclerosis, with subsequent lesions of the kidneys and heart, or be due to some intercurrent affection, tuberculosis in particular.

Certain remedies may also give rise to albuminuria.

The prognosis and treatment of albuminuria, therefore, depend entirely on the origin and causes of it, and the reader is referred to the various diseases in which it occurs as a symptom.

> Investigations showing the existence in many cases of a direct relationship between the acid content of the urine and the amount of albumin and tube casts present. In the first case of albuminuria, the administration of phosphoric acid was found to cause an immediate increase in the albuminuria. In other words, with an increased acidity of the urine, there was a corresponding increase in the amount of albumin. On the administration, however, of alkalies in place of the acid, the albumin and tube casts diminished and finally disappeared. All the cases which were examined showed that, with increased acidity, there was increased albuminuria, and, corresponding with a diminution in acid, there is a diminution in the albuminuria. At the same time, in all cases of advanced grave kidney trouble, and especially in uremic patients, the relationship to acidity cannot always be demonstrated. The writer goes on to show that not only is the albuminuria lessened by alkali administration, but the functioning of the kidney is greatly improved and the very important excretion of chlorides is accelerated. The best mode of administration of the alkali is in the form of the ordinary sod. bicarb., which must sometimes be given in large doses. V.

Hoesslin (Münch. med. Woch., Aug. 17, 1909).

Albuminuria is most constant after operations on the abdominal, genital and urinary organs. In case of pre-existing kidney lesions rapid operating is necessary. The general anesthesia kept up for an hour or longer might prove fatal just as well without any operation, other things being equal. The writer observed albuminuria after accidental traumatism, showing that the shock is the main factor rather than the anesthetic in postoperative albuminuria. Satre (Paris méd., May 26, 1917).

The writer calls attention to a form of chronic nephritis with albuminuria which is often insidious and found in apparently healthy persons in the course of routine examinations. The same affection has also been classed among the cyclic or orthostatic albuminurias of adolescents. The features are those of a non-progressive nephritis with small amounts of albumin, occasional granular and hyaline casts, and a normal phenolsulphonephthalein excretion. Such cases usually show no obvious cause of the nephritis and albuminuria, but on careful examination there will be found to be some chronic focus of infection, such as the tonsils, kidney stone, etc., removal of which leads in a few months to complete recovery of normal kidney function with freedom from albumin and casts in the urine.

Several illustrative cases are given by the writer. In one of these the infection was bronchial and the staphylococcus was isolated from the sputum. The administration of a vaccine cured both the infection and the nephritis. Dental abscesses are also very frequent foci of infection which lead to these forms of nephritis. While recovery follows the removal of all foci of chronic infection, its progress may cover several months, during which the irritation of the kidneys is being gradually repaired. David Riesman (Jour. Amer. Med. Assoc., Dec. 15, 1917).

TESTS.—By means of the tests commonly employed the presence of albumin in the urine is revealed, but no attempt is made to discern between the different proteids; the differential diagnosis between the serum-albumin, globulin, etc., will be given later on.

The sample of urine to be examined must be very limpid without deposits of any kind; if this be not the case, the urine should be filtered previous to the examination, because a slight cloud of coagulated albumin will only be discernible when the fluid is very clear before the reagent has been added. When the urine contains many bacteria, even repeated filtration will be insufficient to make it clear; this can then be done, however, by addition of a solution of sulphate of magnesia and of carbonate of soda. By shaking the mixture a precipitate of carbonate of magnesia is formed, and when this is removed by filtration the filtrate will be perfectly clear. In many cases a few drops of caustic soda will clear the urine, but urine treated in this manner will not give a precipitate of albumin by boiling, while the test of Heller is practicable also in this case.

Test by Boiling.—A few c.c. of urine are heated to the boiling point and some (5 to 10) drops of nitric acid added. When the urine is acid the albumin will ordinarily coagulate by boiling alone and precipitate as a whitish powder or in small flakes. The nitric acid is nevertheless in all cases to be added, as well in order to complete the precipitation of albumin as to avoid mistakes caused by the presence of a precipitate of phosphates or carbonates,—which will immediately dissolve when nitric acid

is added. This test is very delicate and will reveal 0.01 to 0.005 per cent. of albumin. Instead of nitric acid, acetic acid can be employed, but, while the nitric acid is to be added after boiling and in a quantity of 5 to 10 drops, acetic acid is added before the boiling, and only a sufficient quantity (1 to 2 drops) should be employed as to make the urine but slightly acid. This is especially necessary when the urine is alkaline, because the alkaline albuminates with a surplus of acetic acid give a compound which is not coagulated by boiling.

Tretrop heats the urine nearly to a boiling point and adds a few drops of a 40 per cent. solution of formalin. The albumin coagulates like white of egg. After pouring off the fluid, the proportion of albumin can be determined by weighing the coagulum left.

Bychowski describes the following simple method to detect the presence of albumin, even if only a few drops of urine can be obtained: One or 2 drops of urine are put in a test-tube of hot water. After shaking, a whitish cloud is formed, if albumin is present. The test is very distinctive and is still more apparent when the test-tube is held against a black background. Of course, phosphates give the same reaction, but the cloud disappears on the addition of a drop of acetic acid.

Test for albumin in the urine in which the extra work of having a control or the filtering of the urine or the modification of its reaction has been eliminated.

Material needed for the test: Saturated salt solution, acetic acid, test-tube, pipette.

On heating urine three substances may be thrown down: albumin, nucleo-

proteid, and phosphates. About 5 to 10 c.c. of saturated salt solution, slightly acidulated with acetic acid, is heated to boiling in a test-tube. The urine to be tested is carefully allowed to run on top of the hot salt solution by means of the pipette. In order to make a good picture, the quantity of urine used ought to equal that of the salt solution.

By means of the heat in the saturated acidulated salt solution the above-mentioned substances are likely to be precipitated, but, owing to the contact, the saturated salt will not let the nucleoproteids appear, while the phosphates are also held in suspension by the acid; hence nothing can appear at the point of contact of the hot saturated salt with the urine except albumin.

Depending on the quantity of albumin present the reaction will be marked or only a film will appear overlying the clear, crystal-like salt solution. It is in urine with a trace of albumin in which this test shows extreme delicacy. The clear, crystal-like salt solution and the control-column of urine above with the surface of contact contrast quite decisively in distinguishing a delicate cloud.

Different pictures are produced in the great variety of urines by means of this technique :—

1. In clear urine which contains no albumin the delicate point of contact where the urine rides the hot salt solution is better brought out by setting the solution in motion by gently shaking the tube to and fro.

2. In clear urine sometimes a cloud appears some distance above the point of contact. This is due to the heat, which, traveling farther and faster than the acid of the salt solution, throws down a phosphate cloud.

3. Cloudy urine due to phosphates or urates is cleared at the point of contact because the acid and the heat dissolve these, respectively.

4. In cloudy urine due to bacteria no change is seen in the urine at the point of contact, and here, at times, only a close scrutiny of the urine above the crystal-like salt solution below in comparison with the zone of contact will give us the correct reading.

5. In urine containing albumin clouded by urates or phosphates, the albumin cloud at the contact differs in density from the remainder of the urine. Often the film of coagulated albumin is so delicate that the clearing of urates or phosphates is again seen above that of the contact zone.

6. In albuminous urine clouded by bacteria the coagulated albumin at the point of contact accentuates its presence by its difference in density.

It is in cloudy urine that the control of a clear, crystal-like liquid below the urine above emphasizes the beauty of the reaction in the zone of contact.

This test is a modification of the saturated salt, or brine, test, yet it adds to this old method the new qualities of diminished labor, simplicity, and accuracy. H. L. Ulrich (Jour. Minn. State Med. Assoc., Feb. 15, 1909).

Method of employing the acetic acid test for the detection of albumin which has long been used in France: 20 c.c. of urine, about three-fourths of a test-tube 1.5 cm. in diameter, are treated with 5 drops of 20 per cent. acetic acid, mixed, and one-half poured into a second test-tube. The contents of one tube are boiled, the other serving as a control. Albumin produces a cloud or precipitate in the boiled tube. Before testing, the urine must, of course, be perfectly clear; if necessary, it is shaken with Kieselguhr and filtered. If the acetic acid causes a cloud in the cold (nucleoalbumin), it is cleared by filtration before boiling. An alkaline urine should be acidulated slightly to prevent the precipitation of the phosphates, or, if a precipitate of phosphates appears when the urine has been treated with acetic acid and boiled, a few more drops of the dilute (20 per cent.) acid may be added to dissolve it. This will not redissolve even a slight albuminous cloud, provided the urine is not boiled again. Glaesgen (Münch. med. Woch., Bd. lviii, S. 1123, 1911).

Heller's Test.—Three to 4 c.c. of nitric acid are poured in a test-tube and a few c.c. of urine are cautiously filtered down along the sides of the tube without shaking the latter. The nitric acid rests on the bottom of the test-tube, and where the fluids are in contact a distinctly limited disk of grayish-white precipitate will appear. When only traces of albumin are present the precipitate will only take place after some minutes. The more or less distinct violet coloring which also appears at the point of contact of the two fluids is due to oxidation of indican or other chromogens. This test is very delicate and reliable; 0.003 per cent. of albumin is revealed by it.

Fallacies.—By the addition of nitric acid the urates or urea are also precipitated; these will not form a limited disk, but render the urine turbid. Resinous acids (copaiba, etc.) are precipitated by nitric acid, but are dissolved by the addition of concentrated alcohol. This error can be avoided by diluting the urine or by moderately warming the nitric acid before the test. Very often also a fine disk or ring will appear above the point of contact. This precipitation is due (Morner) to the presence of nucleoalbumins (mucin, chondrolin, sulphuric acid, etc.) and is more distinct after dilating the urine.

Test by Acetic Acid and Potassic Ferrocyanide.—The urine is rendered acid by acetic acid, and some drops of a solution of potassic ferrocyanide are added. This reagent, the serum-albumin, the globulin, and the albumoses are precipitated, while none of the normal constituents of the urine are (Huppert).

Heynsius's Test.—A still more delicate test than Heller's is that of Heynsius, by acetic acid and sulphate of soda. The urine is rendered acid by acetic acid, and an equal volume of a saturated solution of sulphate of soda (or of common salt) is added. The mixture is boiled, and all kinds of albumin will then be precipitated in white flakes.

The Magnesium-nitric Test (Roberts's).—One c.c. of nitric acid is mixed with 5 c.c. of a saturated solution of sulphate of magnesium, and a small quantity of this mixture is added to the urine. The albumin will be precipitated as a distinct ring.

Metaphosphoric Acid (Hindenlang's) also precipitates albumin in the same manner as nitric acid; but this test is not as delicate as that of Heller. The solution of metaphosphoric acid must be freshly prepared for use, as the solution easily changes to orthophosphoric acid upon standing, which does not precipitate albumin.

Picric Acid Test (Johnson's).—A few drops of a saturated solution of picric acid will cause a white precipitate when albumin is present; this test is only indicative of the presence of albumin, however, when the precipitate appears immediately. The urine must be acid. After some time the uric acid and the creatinine will also be precipitated (Jaffé).

Fallacies.—By addition of picric acid and peptones, the resinous acids,—such as those of copaiba,—and alkaloids—such as morphine—are precipitated.

Perchloride-of-mercury or Spiegler Test.—A solution of 8 grams of mercury, 4 grams of tartaric acid, 20 grams of glycerin in 200 grams of water produces a precipitate of albumin. The test is carried out in the same manner as Heller's test. It is very delicate (it reveals 0.0002 per cent. of albumin), but is not reliable when the urine is poor in chlorides (Jolles).

Millon's Test.—A solution of nitrate of mercury is added to the urine and the mixture heated to boiling. Nitrate of potash is then added; the albumin presents as a precipitate of red flakes. This test is disturbed by the sodium chloride of the urine and will be much better if tried upon the precipitate after boiling the urine.

Tanret's Test.—The reagent of Tanret is composed of perchloride of mercury, 135 grams; iodide of potash, 3.32 grams; glacial acetic acid, 20 c.c; distilled water, sufficient to make 100 c.c.

Some drops of this mixture are added to the urine, when it will coagulate the albumin. It will also, however, precipitate the urates.

Tognetti described a "tannohydrochloric" test which reveals albumin, even in a proportion of 1 to 2,000,000. An equal amount of 1.5 per cent. alcoholic solution of tannin is added to the urine. After heating, an equal amount of 33 per cent. hydrochloric acid is added. A yellowish-white precipitate is gradually thrown down.

Colquhoun recommends a solution of carbolic acid in absolute alcohol; this gives a white, milky precipitation of albumin. The test is said to show 0.002 per cent. albumin.

Many other reagents have been recommended, which cannot be mentioned in detail. The boiling test, Heller's test, the potassic ferrocyanide test, and the picric acid test are the most practicable and quite sufficient in general work.

> After illustrating the disadvantages of various procedures hitherto widely recommended, the writer advocates, after extensive clinical experience, a **diaphanometric method.** In preparing the necessary standard solution, the albumin content of a given albuminous urine is first accurately measured by the weighing method. Some of the urine, previously filtered, is then diluted with a solution consisting of sodium chloride, 7.5 grams, and mercury cyanide, 1 gram, in distilled water, enough to make 1 liter, until it contains 1 gram of albumin per liter. In successive test tubes of equal diameter are now placed respectively, 0.5, 0.7, 0.8, 0.9, 1.0, 1.2, 1.4, 1.6, 1.8, and 2 mils of the resulting mixture, and the fluid in each tube made up to 10 mils with the chloride cyanide solution. The various tubes thus correspond to samples of urine containing from 0.05 to 0.8 gram of albumin per liter. To each tube is added 2 mils of a 20 per cent. solution of trichloracetic acid. A turbidity of increasing intensity in the successive tubes is thus produced. After being shaken, the tubes are carefully stoppered or sealed and labelled. File marks at 10 and 12 mils are now made on an additional tube of the same diameter as the standard series. In testing urine, a test for gross albumin content is first made by the qualitative method and the urine, if necessary, diluted with saline solution so as to contain from 0.05 to 0.2 gram of albumin per liter. The urine is then placed in the empty tube up to the 10-mil mark, trichloracetic acid solution added up to 12 mils, and the mixture shaken. The standard tubes are now all shaken and the urine mixture under test compared with the standards until an equal degree of turbidity is found. Bauzil (Jour. Amer. Med. Assoc., from Paris méd., Oct. 5, 1918).

Xanthoprotein Test.—Albuminous urine heated with a surplus of concentrated nitric acid will take a yellow color, and some of the albumin coagulates in yellow flakes, which are soluble in alkalies with an orange-red color.

> Very minute quantities of albumin may be detected in the urine by means of the deviation-of-complement test. For antigen the writer has used the serum of rabbits which had been immunized against human blood-serum.

When albuminous urines were diluted to such a point that they no longer gave a reaction with heat and acetic acid or with nitric acid, they still yielded positive results by the complement-deviation test, while in many instances albumin could be detected by this method in diluted urine when it could not be demonstrated by the ordinary chemical tests. The deviating power of the urine is not affected either by filtration through a Berkefeld filter or by dialysis. The antibody of the urine was, moreover, found to reside entirely in the serum albumin and serum globulin, and after the removal of the substances from the urine the remaining fluid no longer had the property of an antibody. C. H. Wilson (Jour. Path. and Bact., vol. xiii, p. 484, 1909).

Following are two new qualitative tests for albumin in urine, which are apparently specific as well as simple. The first test is with tincture of iodine and sodium bisulphate: A few c.c. (5 to 6) of the urine—which must, of course, be clear—are placed in a test-tube and acidified with a few drops of dilute acetic acid. About ⅕ volume of tincture of iodine (10 per cent.) is now added, and the whole is well shaken. A dirty, dark-brown precipitate results. A saturated solution (watery) of sodium bisulphate is next added drop by drop, shaking constantly, until the brownish fluid is decolorized. If the urine contains albumin, one sees a permanent whitish cloud or flocculent precipitate. If no albumin is present, the fluid remains clear after the addition of the sodium bisulphate, and shows only the original urinary color. With minimal quantities of albumin, the reaction becomes more evident on standing a few minutes. The second is with decolorized tincture of iodine: One decolorizes tincture of iodine with saturated watery solution of sodium bisulphate and filters. The filtrate is a clear, rather yellowish fluid, which keeps well. On standing for some time, small, yellow crystals may be precipitated, without injury to the reagent. The urine, as in the first test, is acidi-

fied with dilute acetic acid. About ⅓ volume of the reagent is added and the whole well shaken. If albumin is present, a cloud or a flocculent white precipitate forms. With traces of albumin the reaction may be delayed a few minutes. Normal urine never shows a cloud with these tests. Oguro (Zeit. f. exper. Path. u. Therap., Bd. vii, S. 349, 1909; Amer. Jour. Med. Sci., Jan., 1910).

In certain cases of profound general intoxication, such as cerebral hemorrhage cases in coma, uremia, and eclampsia, addition of 1 drop of urine to dilute, almost boiling Fehling's produces a deep purple color. Blood serum gives the same reaction as do other proteins that are breaking down to proteoses and peptones, i.e., substances giving the pink biuret test. Nine out of 10 cases seen which gave the test, died. H. Bieler (Jour. Labor. Clin. Med., v, 459, 1920).

Transportable Reagents for Albumin.—Hoffmann and Aazette employ strips of test-paper previously placed in a solution of the double iodide of potassium and mercury until saturated, then removed and dried. Geissler's albumintest paper is previously placed in a solution of citric acid. The urine which is to be tested should be clear and rendered acid by means of a few drops of acetic acid. If there be albumin present, upon immersion of a slip of paper in the urine a distinct precipitate will appear.

Pavy recommends test-pellets containing ferrocyanide of soda and picric acid; when albuminous urine is well shaken with a parcel of the pellet, albumin will be precipitated. Stütz and Fürbringer employ capsuloids of gelatin filled with perchloride of mercury, sodium chloride, and citric acid. The relative delicacy of the tests most frequently employed is graphically represented by Unger-Vetlesen, in the

diagram shown below. The longest columns indicate the most delicate tests.

Quantitative Tests. — The only method which gives fully reliable results is the gravimetric method. One hundred c.c. of urine are boiled upon a water-bath half an hour; if precipitation does not take place a few drops of a weak solution of acetic acid are added; the liquid is now brought on a weighed filter and the precipitate

Esbach employs an albuminimeter, *i.e.,* a graduated glass tube; this tube is filled to one mark (U) with the urine and then to the mark R with the test-solution consisting of picric acid, 10 grams; citric acid, 20 grams; water, 1 liter. The tube is then closed with a rubber stopper and the contents cautiously mixed (not shaken). The mixture is allowed to stand undisturbed for twenty-four

	12	24	36	48	60	72	84	96	108
Ferrocyanide of potassium and acetic acid									
Solution of picric acid									
Test-paper									
Solution of sulphate of soda and acetic acid									
Heller's test									
Picric acid in crystals									
Magnesium-nitric test (Roberts)									
Trichloracetic acid									
Metaphosphoric acid									
Boiling and nitric acid									

repeatedly washed with hot water. The filtrate must once more be acidulated with acetic acid and boiled again, in order to ascertain whether the precipitation has been quantitative. When the water has been removed from the filter by strong alcohol, and the alcohol with pure ether, the filter is dried at a temperature of 110° to 120° C., and the percentage of albumin determined by weighing.

For clinical use several approximate methods have been invented.

hours and the quantity of precipitated albumin then read off. The reading indicates in grams the amount of albumin per liter. The urine must be acid, the specific weight should not be more than 1006 to 1008, and the temperature of the room approximately constant (15° C.). Resinous acids must be extracted with ether. The yellow crystals often found on the side of the glass are crystals of uric acid.

Christensen recommends another method: the albumin contained in 5

c.c. of urine is precipitated by 10 c.c. of a watery solution of tannic acid (1 per cent.). The albumin having been precipitated, 1 c.c. of an ordinary gum-arabic mucilage is added, the volume brought up to 50 c.c. with water, and the whole converted to an emulsion by agitation. Upon a piece of white paper, ruled with black lines 0.5 mm. wide and at equal intervals, is placed a cylindrical glass measuring 4 cm. in diameter. This is half-filled with water, and as much of the emulsion run in as possible without obscuring the black and white lines beneath the vessel. From the number of cubic centimeters required, reference to a table of calculations arranged by Christensen furnishes the proportion of albumin present in the emulsion. When the urine is alkaline it should be faintly acidified with acetic acid before the precipitation of albumin. This test can be made as well by daylight as by the light of a good lamp, and requires only ten or fifteen minutes; but is not applicable to urine containing a small amount of albumin, the variations amounting to two-thousandths.

The polariscope is sometimes employed to estimate the quantity of albumin, but this test is not reliable. It is true that albumin is levorotatory, but this is also the case with normal urine, and sometimes the color of the urine is too dark to allow the use of the polariscope.

Goodman and Stern have pointed out (1908) a quantitative method which gives results in a few minutes. It is based on the precipitation of albumin by phosphotungstic acid in the presence of a mineral acid. One gram of crystallized egg-albumin is dissolved in 100 c.c. of distilled water (solution A); 1 c.c. of this solution is diluted with 9 c.c. of distilled water (solution B). Drop in a test-tube 5 c.c. of the following solution:—

℞ *Phosphotungstic acid* .... 1.5 Gm.
   Hydrochl. acid (conc.) .... 5 c.c.
   Alcohol (95 per cent.)..q. s. ad 100 c.c.

Now it takes 0.1 cm. (added with a pipette graduated in 0.1 c.c.) of solution B to cause a cloudy precipitate, *i.e.*, 0.0001 Gm. of albumin. The diluted urine is tested in the same manner.

For the quantitative determination of albumin in the urine a simple test is recommended by the writer. He uses a round albuminometer. In this he places the urine and the Esbach reagent and adds thereto 0.1 to 0.2 Gm. of barium sulphate (tungspat); after mixing, the glass is set aside for precipitation. In 4 minutes it is complete. A urine containing over 2 per thousand albumin should be diluted before using the test. Anderson (Ugeskrift for Laeger, Apr. 26, 1917).

By the various tests above mentioned, qualitative as well as quantitative, the different coagulable proteids contained in the urine are precipitated; it is rarely of any use to differentiate them one from another.

Globulinuria. — Pure globulinuria without the simultaneous presence of serum-albumin does not occur. In order to precipitate the globulin alone the urine is rendered alkaline with solution of ammonia, after some time filtered, and the filtrate mixed with an equal volume of a saturated solution of sulphate of ammonia. If globulin be present a flaky precipitate will appear.

[The same result can be obtained by using a solution of sulphate of magnesia, which does not precipitate the other proteids of urine, or by diluting the urine until it reaches

a specific gravity of 1002 and leading a slow current of carbonic acid through it for two or four hours. After twenty-four to twenty-eight hours the globulin will be precipitated. Levison.]

Colorimetric Type. — Autenrieth and Mink (Münch. med. Woch., Oct. 19, 1915) comparing the quantitative findings by *colorimetry* with other techniques obtained further confirmation of the precision of the colorimeter technique.

[A colorimetric method of quantitative albumin estimation suitable for the practitioner's use is described by W. Autenrieth and F. Mink (Münch. med. Woch., Oct. 19, 1915) as follows: Ten c.c. of clear or filtered urine in a test tube are heated for a few minutes on the boiling water bath. If a precipitate forms, 2 to 4 drops of dilute acetic acid are added and the tube put back in the water bath. Usually at once, but sometimes only after a few minutes, the albumin all comes down in large flocculi. If the formation of the flocculi is difficult because of the urine being poor in salts, 2 to 5 c.c. of saturated sodium chloride solution should be added. The precipitate is then at once placed on moistened filter paper and washed with about 20 c.c. of hot water, the latter having first been used to rinse out the test tube. The precipitate is next placed in a small funnel over a 10 c.c. graduate. Two to 3 c.c. of 3 per cent. sodium hydroxide solution are placed in the test tube to dissolve the remaining traces of albumin, and then over the precipitate itself, most of which easily goes into solution. Additional 2 to 3 c.c. portions of the alkali are now used, until the albumin is completely dissolved and the total amount of solution is about 9.5 c.c. Four or 5 drops of 20 per cent. copper sulphate solution are now added, the graduate filled to the 10-c.c. mark with alkaline solution, and the mixture well shaken up for two or three minutes. After allowing it to stand five or ten minutes, a clear supernatant fluid suitable for colorimetric examination will usually be found; if not, the mixture may be filtered through dry filter paper, the first few drops being discarded. The solution having been placed in the glass trough of the Autenrieth-Koenigsberger colorimeter, comparison is made 5 or 6 times with the wedge-shaped color scale of the instrument until 2 or 3 readings correspond. The final reading is then referred to a curve chart, which shows the number of milligrams of albumin in the 10 c.c. of urine. The method is held to be very accurate. Where the urine is believed to contain less than 1 gram of albumin per liter 20 c.c. instead of 10 c.c. of urine shoul. be used, and where it exceeds 4 grams, only 5 c.c.

Lewin (Med. Klinik, July 13, 1913) emphasizes the delicacy and reliability of the color reaction which follows when dissolved albumin is treated with a mixture of 0.1 to 0.15 parts trioximinomethylen in 100 parts crude sulphuric acid. Even a 0.02 per cent. solution of egg albumin shows the characteristic violet tint.

In the colorimetric method of Claudius, of Copenhagen, as described by Kahn and Silberman (N. Y. Med. Jour., Oct. 3, 1914) the urine is first filtered and its reaction tested to see if it is neutral or slightly acid. It is then diluted with an equal portion of a 2 per cent. sodium chloride solution. To 5 c.c. of the diluted urine, add now 5 c.c. of Claudius's reagent, which consists of 2 per cent. trichloracetic acid, 0.5 per cent. tannic acid and 0.1 per cent. acid fuchsin. The mixture of urine and reagent is then well shaken in a stoppered 15- or 20- c.c. flask, filtered, and the filtrate compared with a standard in the Sahli or Gowers hemoglobinometer.

Norgaard (Ugeskrift for Laeger, Nov. 25, 1915) has been giving Claudius's quantitative colorimeter test for albumin a thorough trial in 100 specimens of urine and in some other organic fluids, and found that by comparative tests, with an albumin content below 1 per thousand there may be a difference up to 10 per cent. of the findings on analysis by weight. With an albumin content above 1 per thousand, the difference could rise to 20 or 30 per cent., averaging 2.5 per cent. C. E. de M. S.]

Miscellaneous.—D iters (Münch. med. Woch., Dec. 12, 1916) heats an ordinary test tube until the bottom is sufficiently soft to allow its being pushed up into the tube so as to make a small ball-shaped or conical depression in its lower end. In this are poured 6 to 8 drops of nitric acid

and the urine poured on top. The turbidity resulting is more distinct than is obtained with the old test tube owing to the increase of light which passes through the fluid.

Benedict (letter to the N. Y. Med. Jour., Nov. 28, 1914) describes the following simple method to estimate the albumin: Boil the urine thoroughly, adding 1 drop of nitric acid. Centrifugate until the precipitate is no longer condensed. The percentage reading is about 6 times the percentage by weight of dried albumin. If the moist precipitate is large, say more than 1 c.c. (16 minims) in a 10-c.c. (2½ drams) tube, which rarely happens, even when urine is said to coagulate entirely, the lower portion of the precipitate is still further compressed. This method is simple and rapid, and is reasonably accurate, sufficiently so for clinical use.

A test described by Osmond (Lancet-clinic, Dec. 13, 1913) is asserted by him to be equal in delicacy to any other, and to have certain features which make it superior to them for routine use. The following solution is employed:

Picric acid .... 5 parts
Citric acid .... 10 parts
Sodium chloride .... 100 parts
Distilled water .... 1000 parts

Technique.—Place 2 or 3 c.c. of the reagent in a test tube. Filter the urine until it is perfectly clear. Then allow urine very gently to float upon the surface of the reagent in the inclined test tube. Albumin will show as a white zone at the line of contact of the two amber fluids, which are practically iso-chromic. D. W. Prentiss (Med. Council, Aug., 1912) gives the following method to record the amount of albumin in urine in such a way that it can be compared with later examinations in the same case, or with other cases. The record is permanent, easy to make, and sufficiently accurate to be of the utmost value to the busy physician: 1. Make the underlying nitric test for albumin, in a test tube. 2. Allow the tube to stand 2 minutes. 3, Hold the tube between a black or dark object and the eyes, on the level with the eyes. 4. Note the exact thickness of the ring of albumin at the line of contact. 5. On the chart draw parallel vertical lines which represent the test tube. Connect these lines by a cross line the exact breadth of the thickness of the coagulated albumin.

H. E. Jones (Glasgow Med. Jour., Jan., 1916) reports a case in which results of albumin determination in the urine with the Esbach procedure proved misleading, owing to a high degree of alkalinity of the urine tested. Although an albumin precipitate was obtained in the heat and acid tests, no precipitate was obtained in the albuminometer owing to the fact that the amount of citric acid contained in Esbach's reagent was insufficient to acidulate the urine to the extent required for precipitation of albumin by the picric acid in the reagent. In all very alkaline urine this source of possible error in the interpretation of the test should be borne in mind.

Lenk (Deut. med. Woch., Oct. 21, 1915) recommends the following rapid test for albumin and sugar. Albumin, enzymes, etc., are absorbed by negative substances like kaolin, charcoal, pulverized pumice stone, etc. If these are mixed with the urine after addition of Esbach's reagent (a mixture of 5 Gm.—75 grains—picric acid with 10 Gm.—2½ drams—citric acid in 500 c.c—1 pint—water) as the particles settle to the bottom of the dish they carry the albumin down with them. Using pulverized pumice-stone, the albumin is precipitated completely in 10 minutes.

An improved technique for Tsuchiya's phosphotungstic-hydrochloric acid-alcohol reagent for detecting albumin in the urine is offered by Sueyoshi (Mitteil. a. d. med. Fakul. d. k. Univ. Tokyo, xiv, No. 3, 1915). The reagent is a mixture of 20 Gm. mercuric chlorid; 5 Gm. potassium bromid; 10 c.c. hydrochloric acid (30 per cent.); water 55 c.c. and alcohol (95 per cent.) to 100 c.c. The test tube is filled about half full of urine and about seven-eighths as much of the reagent is poured in and thoroughly mixed with it. The albumin sediment is measured next day as usual.

According to the writer, the formation of picric acid crystals in 10 c.c. of urine treated with 5 c.c. of Esbach's reagent is a delicate test for albumin. A positive response throws light on the prognosis. The crystals are found more numerous as recovery progresses, either in acute or chronic

kidney disease. The changes in the proportion of crystals always foretell the next stage of the disease. Bergell (Zeit. f. klin. Med., xc, No. 5-6, 1921).

TREATMENT.—T. C. Janeway (Amer. Jour. Med. Sci., Feb., 1916; N. Y. Med. Jour., Feb. 12, 1916) stated that for the most part treatment in the past was purely schematic, based on a conventional diagnosis, and usually involved violent interference with the habits of a lifetime. To tell every patient with albuminuria or hypertension to stop eating red meat, or, worse, to go on a diet, is evidence of ignorance. He divided the cases into 5 types.

The *first type* is one in which *albumin and casts in the urine are the only evidence of disease.* If the treatment of acute nephritis results in a steady subsidence of albuminuria, it should be persisted in, just as though the patient had a known acute nephritis, but if a week in bed on a milk diet has no appreciable effect on the albumin and casts, the bed and milk diet are an unwarrantable hardship. In children the question of a *postural albuminuria* should be cleared up without delay. The effect of exercise and cold baths should be studied carefully, as these may cause an albuminuria. Severe physical strain, exposure to cold and wet, and excesses, not only in tobacco and alcohol, but in other things as well, are to be avoided. Soups and spices may wisely be excluded from the diet. Gourmands should have their excessive appetites restrained; obese patients should be moderately reduced; but if the phthalein test is normal he sees no reason for a restriction of protein, either qualitative or quantitative, below a moderate normal intake. Patients who use much salt should reduce it.

The *second type* is one in which *the patients have hypertension with or without a trace of albumin and with slight if any subjective symptoms.* The worst advice for a man of important affairs is to give up business completely, but change of occupation may be imperative for the manual laborer. It is of great importance to secure adequate normal sleep. A short rest in the middle of the day is of great benefit. Tobacco in excess is a poison. While excessive athletics may be dangerous, exercise is beneficial, and when this cannot be allowed for any reason, massage is helpful. Diet should follow about the same lines as in the first class, and the use of salt should be moderate. The abuse of fluid is dangerous and a winter vacation in a warm climate is sometimes desirable.

The *third type* is that in which *hypertension and outspoken myocardial insufficiency* are present. The heart must be safeguarded by rest in bed or in a chair. Those with auricular fibrillation need **digitalis**, those without should also receive the drug, but some of them do not respond as well. Toxic effects must be watched for, as some patients with regular rhythm are made worse by digitalis. Then one of the **caffeine** diuretics should be tried, **theocin**, about 12 grains (0.77 Gm.) a day, or **diuretin**, about 40 grains (2.6 Gm.) in divided doses, not oftener than every other day. The fluid intake and the urine output must be measured accurately. Diuresis from digitalis should not be expected within 48 hours, but that from the caffeine group may be observed on the day of administration and the next doses should be given when the diuresis ceases. The symptoms that demand treatment are dyspnea, edema, and the whole picture of cardiac fail-

ure with passive congestion of the viscera; vasodilators are indicated. He speaks highly of **fresh nitroglycerin tablets** dissolved on the tongue and not swallowed.

Theobromine has been found to give good results in some cases. **Regulation of the diet** and **reduction of fluids and salt** are indicated.

The *fourth type* is one of *general edema without notable myocardial insufficiency.* These patients excrete small quantities of salt, so treatment should always begin with a period of very low salt and water intake to promote rapid absorption of the dropsy. Bed is desirable until normal function is restored, and if the dropsy disappears the further treatment is that of convalescence from acute nephritis. Obstinate edema requires other dehydrating measures, **sweat baths, hot packs,** perhaps **purging.**

The *fifth type* is that of *advanced renal insufficiency.* Treatment is purely symptomatic. Paroxysms of dyspnea and of Cheyne-Stokes breathing demand special relief. **Morphine** is effective in many cases, but may induce anuria with coma. **Chloral hydrate** in 5- or 10- grain (0.3 to 0.6 Gm.) doses, alone or with **bromides,** sometimes is effective. The patients should be encouraged to sleep in a chair instead of insisting that they go to bed.

Diet should be reduced to a minimum by the patient himself. **Bleeding** has its greatest value in sudden convulsions, when the removal of 500 or 600 c.c. of blood is indicated. **Sweating** occasionally is of benefit.

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AND
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ALBUMOSURIA.—Albumose occurs in the urine under various circumstances. It may appear when large quantities of pus, such as in empyema, a large abscess, etc., accumulate in any region; in chronic suppurative processes, intestinal, peritoneal, meningeal, etc.; in pyogenic nephritis, and when there is a considerable destruction of white corpuscles. It may also indicate a more or less rapid tissue disintegration, caused by pathogenic organisms, as in pneumonia, particularly in the resolution stage; hepatic disorders, especially acute yellow atrophy. This form is usually temporary.

The writer has encountered albumosuria in five pregnant women. It always disappeared a few days after delivery and did not seem to have any pathologic or prognostic import. Tanberg (Norsk Mag. f. Laegevidenskaben, Jan., 1918).

Case in a woman of 39 years, the outstanding points of which were the presence of the albumose in the urine, with a relative and total increase of small lymphocytes in the blood, and the absence of any signs of malignant growths, and cardiac enlargement, with murmur, and dropsy in the legs, together with the presence of streptococci in the urine. Heimann and Wilson (Lancet, Dec. 28, 1919).

In a rare form known as *"myelopathic albumosuria* or *Kahler's disease,"* characterized by a copious excretion of Bence-Jones proteose, the latter is persistent, and is usually associated with sarcomatous degeneration of the bone marrow. This form runs a rapid course and is invariably fatal. A. Graham-Stewart (Clinical Jour., Mar. 29, 1916) observed 3 cases of albumosuria in children due to intestinal toxemia, with mucous colitis in one of the patients. Toxemia of intestinal origin is regarded by the author as an unrecognized cause of albumosuria. He urges the importance of an early distinction between the latter and albuminuria. Heller's test for albumin then gives a bulky precipitate. This does not form with nitric acid so definite a ring as does albumin. It is more woolly and tends to

float to the top. It may at once be distinguished from albumin by heating when the ring or cloud disappears to reappear on cooling. Again the ordinary heat test does not cause albumose to form a cloud.

Martindale gives the following tests for the detection of albumoses: Acidulate the specimen with acetic acid, and add 10 per cent. potassium ferrocyanide solution. This precipitates pri ary albumoses. This ferrocyanide precipitation distinguishes albumose from compound protein. On warming, the precipitate dissolves, to reappear on cooling. This distinguishes it from that due to serum albumin.

Again, after precipitation by salicylsulphonic acid, albumoses dissolve on heating and reappear on cooling.

There is also the Biuret reaction. Albumin is tested for by Heller's test; if present, it is removed by 10 per cent. trichloracetic acid solution and the Biuret test applied to the filtrate. To do this, 1 drop of a 2 per cent. copper sulphate solution is placed in a test tube; 5 c.c. of the urine are added, and then 5 c.c. of a 10 per cent. solution of sodium hydroxide. The presence of albumose is indicated by a rose pink.

As regards the *Bence-Jones form*, Martindale states that this albumose is detected by: Coagulating at 58° C., *i.e.*, lower than serum albumin, which coagulates at 75° C.; precipitates with hydrochloric acid; precipitates with nitric acid in the cold; on raising to the boiling-point, however, the coagulum dissolves more or less completely, and reappears on cooling; precipitates with potassium ferrocyanide and citric acid (often takes time to develop, differing in this respect from albumin).

The hypochloric acid test is stated to be very sensitive, and not to depend on excess of salts. The result is obtainable after very free dilution of the specimen.
                                        S.

ALCOHOL.—Alcohol is one of a group of hydrocarbon compounds which have as their base a radical designated as ethyl, chemically represented by the formula C_2H_5. Alcohol is a hydrate or hydroxide of ethyl—C_2H_5OH.

To distinguish it from other more toxic members of the series of alcohols, particularly fusel oil (chiefly amyl alcohol) and wood spirit (methyl alcohol), the spirit used in medicine is called ethyl alcohol. It is obtained by distillation and subsequent purification from a fermented mash of potatoes or grain, from fermented sugar, or from wine, and is known in the British Pharmacopeia as rectified spirit.

Absolute alcohol, *i.e.*, alcohol at least 99 per cent. pure, occurs as a volatile, inflammable, colorless liquid, with a characteristic pungent odor and burning taste. Its boiling point is 172° F. (77.7° C.). It has a marked affinity for water, which it abstracts from whatever substances it may be in contact with, including the air and the human tissues. It is miscible in all proportions with water, glycerin, ether and chloroform. When absolute alcohol is mixed with water the resulting volume of fluid is slightly less than the sum of the two components before their admixture.

Alcohol is a solvent for resins, volatile oils, fats, and alkaloids, and is very extensively employed as such in preparations containing remedies of these classes, most of which are insoluble in water. It forms the menstruum in the official tinctures, spirits, elixirs, and all but two of the fluidextracts.

PREPARATIONS AND DOSE.

Alcohol contains 94.9 per cent. by volume (92.3 per cent. by weight of pure ethyl alcohol to 5.1 per cent. of water). Specific gravity, 0.816. Rarely used internally in doses of 1 to 4 drams, diluted with water.

Alcohol Dehydratum (Absolute Alcohol) contains not more than 1 per cent. of weight of water. Specific gravity, 0.797.

Alcohol Dilutum (Diluted Alcohol).—A mixture of alcohol and distilled water, containing 48.9 per cent. by volume (about 41.5 per cent. by weight) of pure ethyl alcohol to 51.1 per cent. of water. Specific gravity about 0.937.

Spiritus Frumenti (Whisky), U. S. P. VIII.—44 to 55 per cent. by volume of absolute alcohol.

Spiritus Vini Gallici (Brandy), U. S. P. VIII.—46 to 55 per cent by volume of absolute alcohol.

Vinum Album (White Wine), U. S. P. VIII.—8.5 to 15 per cent. by volume of absolute alcohol.

Vinum Rubrum (Red Wine), U. S. P. VIII.—8.5 to 15 per cent. by volume of absolute alcohol.

Whisky is produced by the distillation of fermented grain (rye, corn, or barley), and brandy by the distillation of fermented grapes. Inasmuch as the toxic amylic alcohol is likely to be present in freshly distilled spirits, the Pharmacopeia specifies that these products shall have been kept in storage for a certain period before use (whisky, two years; brandy, four years), the amylic alcohol becoming oxidized into harmless ethers. White wine results from the fermentation of the juice of fresh grapes, from which the skins, seeds and stems have been removed, while red wine is produced from purple-colored grapes with the skins included. The latter contains more tannin, but less tartaric acid than white wine.

Dose.—The ordinary dosage of whisky or brandy in adults unaccustomed to their use may be said to range from 1 dram (4 c.c.) to 2 ounces (60 c.c). In regulating the dose the capacity of the individual to oxidize the alcohol is to be taken into account, the object being, if alcohol is to be given repeatedly, to limit the amount to that which can be destroyed in or eliminated from the organism in the interval between successive doses. According to Bartholow, the quantity which a healthy adult is able to oxidize in twenty-four hours is from 1 to 1½ ounces of absolute alcohol. Where this is exceeded, an accumulation of the drug in the system is likely to occur, and the following symptoms may be expected to appear. Flushing of the face, dryness of the skin and mucous membranes, bounding pulse, and the odor of alcohol on the breath. Such signs indicate, in any given case, that the useful amount of alcohol, whether employed for general or merely for digestive stimulation, is being exceeded. In persons habitually taking alcoholic beverages the ability to oxidize alcohol is augmented, finding its expression in increased tolerance; hence in these individuals, if alcohol is given for the purpose of obtaining therapeutic effects, the dose will have to be increased, and even, in many cases, doubled or tripled. In febrile states large amounts have often been administered without causing signs of intoxication, the oxidizing power evidently being heightened during the febrile process; notwithstanding this fact, it is now generally considered that small doses of alcohol—if, indeed, it be used at all in these cases other than during periods of dangerous circulatory depression—will give as good results as large amounts.

In children, as well as in the aged, alcohol is well borne. To the former it can be administered in doses proportionally larger than are suitable for adults, while in the latter the dose need not be reduced from that given to the middle-aged.

MODES OF ADMINISTRATION.—Alcohol, as used in therapeutics, is usually exhibited in dilute form in one

of the various spirituous beverages, none of which is now official. They may conveniently be grouped according to the percentage of alcohol contained.

The so-called "spirits" include whisky, brandy, gin, rum, and arrack, and all contain about 50 per cent. of alcohol. A liquor having this percentage is said to be "proof spirit," implying that it contains just sufficient alcohol to be inflammable. Gin ("spiritus Genevæ") is made by adding oil of juniper berries to rectified alcohol or whisky. The official *spiritus juniperi compositus,* with 4 per cent. of juniper oil as well as other flavoring substances, is a preparation similar to gin, but is stronger in alcohol, containing 70 per cent.; the average dose is 2 drams. Rum ("spiritus Jamaicensis") is obtained by distilling fermented molasses or sugar. Like gin, it is not official. Arrack results from the distillation of fermented rice. Spirits contain a large number of other volatile bodies besides the main component, ethyl alcohol. These include higher members of the same group of alcohols as ethyl alcohol, as well as alcohols of other series and a group of bodies the composition of which remains obscure, known as the œnanthic ethers, and which, though present in small amounts, give to the various liquors their characteristic flavors. Spirits differ radically from wines in that they are free of non-volatile compounds, which are left behind in the process of distillation.

The heavy wines contain about 20 per cent. of alcohol, being made from grapes having a large proportion of sugar. They include port, sherry, Madeira, Marsala, Malaga, and others. Port (formerly official as "vinum portense") is a sweet, red wine, containing 15 to 22 per cent. of alcohol; its sweetness is due to arrest of the process of fermentation while still incomplete. Sherry ("vinum Xerici") is a white wine, containing 15 to 18 per cent. of alcohol. Port and sherry of American production are usually lighter, the percentages ranging from 10 to 18. Madeira is a dark-colored white wine with 18 to 22 per cent. of alcohol. Marsala is a wine similar to Madeira, but of Sicilian production. Malaga is a sweet wine, having 17 per cent. of alcohol. The heavy wines are, in general, too sweet for the use of sick persons; when obtained "dry" (free, or nearly free, from sugar), however, they are frequently of benefit to convalescents and to the debilitated.

The light wines contain from 5 to 15 per cent. of alcohol. Ordinary claret ranges from 6 to 12 per cent. This group also includes Burgundy, the Rhine wines, Moselle, Tokay, champagne, and hock, in all of which the percentage of alcohol is usually between 9 and 14. Champagne, though it contains only about 10 per cent. of alcohol, has a pronounced stimulating effect on the gastric mucous membrane because of the large amount of carbon dioxide it liberates. Wines are more slowly absorbed than alcohol, and the physiological effects of the alcohol they contain are correspondingly less marked. In addition, wines possess distinct nutritive value, by virtue of the numerous substances, both organic and mineral, which they embody. These include, according to an analysis of red wine by Gautier, albuminoid, fatty, and carbohydrate constituents, glycerin, potassium tartrate, succinic acid, acetic, citric, malic and carbonic acids, and salts such as the chlorides, bromides, iodides, fluorides, and phosphates of potassium, sodium, calcium and magnesium oxide of iron, etc. Wine also contains a number of

volatile bodies, such as are present in brandy in larger amount. Light wines are useful wherever prostration is or has been a marked feature of the case, *e.g.*, in **typhus, intermittent fever, scurvy, and cholera** among the more acute diseases; also in many chronic affections, excluding, however, cases of Bright's disease, chronic digestive disorders, neurasthenia, anemia, and diabetes. Wines are peculiarly liable to undergo acetic fermentation in the stomach (Hayem), and hence are not well borne in certain gastric disturbances. It has been found *in vitro* that wines uniformly interfere with peptic digestion. Red wines very usually disagree where there is gastric hyperacidity. In these cases white wines are generally serviceable. White wines have a diuretic effect beyond that possessed by the red wines. When very acid, however, they are in themselves capable of causing gastric disorders, and should be avoided wherever diarrhea exists. Many of the Rhine wines are not suited to those having a tendency to the formation of oxalic deposits, owing to the oxalic acid which they contain.

Malt liquors (beer, ale, brown stout, porter) contain less alcohol but have greater nutritive value than any other of the alcoholic beverages. They are produced by causing an extract of malt (sprouted barley grains) and hops to undergo fermentation by the yeast-plant. The malt is previously allowed to germinate, in order that the starch it contains shall be transformed into the more easily fermentable sugar. The diastase which effects this conversion is formed by the grain itself during germination. The yeast then ferments the sugar with the production of alcohol. The final product contains about 3 to 7 per cent. of alcohol and a large percentage of solid constituents available for nutrition, including mainly dextrin, sugar; albuminoid, fatty and gummy substances; succinic, lactic and acetic acids; aromatic and bitter principles derived from the hops, carbon dioxide to the extent of 6 to 8 times the volume of the liquor, and a number of salts resembling those found in the ashes of meat extract, principally phosphates and salts of potassium and calcium (Manquat). Beers also contain diastase, which aids in the digestion of carbohydrate foods and tends to produce obesity. Ale differs from beer in that its fermentation is carried on at a high temperature instead of a low one; it usually has a higher percentage of alcohol, ranging from 4 to 8 or 9 per cent., while beer has 2 to 6 per cent. (4 per cent. on the average). Porter and brown stout are fermented at a still higher temperature; some of the sugar is converted to caramel, giving these beverages their darker color. They contain 4 to 6 per cent. of alcohol.

When the digestive powers are but little impaired, beer is valuable as a tonic and nutritive. The hops and the carbon dioxide probably both stimulate functionally the gastric mucosa. Where the digestion is weak, the large dextrin and sugar content of beer may undergo fermentation in the stomach. The absorption of beer is, in any case, slower than that of other liquors. Beer diluted with water is said to be better borne than wines where there is hyperchlorhydria. The low percentage of alcohol contained in beer renders it useful where the patient appears specially sensitive to the action of alcohol on the cerebrum. A syrupy extract of malt is official in the United States Pharmacopeia as *extractum malti;* it contains

large proportions of dextrin, sugar, phosphates and nitrogenous bodies, and but 2 per cent. of alcohol.

Less important medically are the wines of other fruits than the grape, and the liqueurs. Among the former may be mentioned cider, which results from the fermentation of apples and contains 2 to 5 per cent. of alcohol, and perry, a similar product made from pears. Cider is useful where diuretic and slightly laxative effects are desired. Liqueurs comprise a large class of alcoholic products differing widely in composition. They are generally made by the addition of essential oils; they frequently contain a large amount of sugar, and are of but little value in therapeutics.

In acute diseases alcohol is usually given internally in the form of whisky or brandy.

Under the Revenue Act of October 3, 1917, which went into effect December 1, 1917, every physician who wishes to buy alcohol U. S. P. for his own use must get a permit from the U. S. Internal Revenue Office, file a bond and state in his application blank for what purpose he intends to use the alcohol. This applies whether it is for washing his hands or for preparing stains for laboratory use, or for any other purpose for which he desires to use grain alcohol without having it medicated or in some manner denatured. A physician cannot purchase more than one pint of alcohol that has been medicated without obtaining a permit. EDITORS.

CONTRAINDICATIONS.—Alcohol is contraindicated in nephritis and inflammatory conditions of the urinary passages, in conditions associated with marked gastric or intestinal irritation, and in persons likely to acquire the alcoholic habit,—especially young adult or middle-aged neurotics, and persons who have been subjected to traumatism of nervous structures. In prolonged cardiac depression alcohol is likely to do more harm than good. Sweet wines and beer are contraindicated in diabetes mellitus and in eczema. In the diarrheas of children alcohol should not be administered unless the stomach and bowels have already been freed from putrefying material.

Syphilis is always badly affected by alcohol, and the latter is responsible for many of the evil results often seen in this disease, both in the skin and in the nervous system. The syphilitic should be an abstainer from alcohol from the moment of his infection. L. Duncan Bulkley (Med. Rec., Jan. 29, 1910).

PHYSIOLOGICAL ACTION.—
The effects of alcohol, when it is taken internally, vary according to the size of the dose. The action here to be described is that of therapeutic or somewhat larger doses.

Digestive Tract.—In the mouth and pharynx, alcohol has a slightly astringent action upon the mucous membranes. For a brief period it also causes an increased flow of saliva, and when in no greater concentration than 5 per cent., has been found by Störck to favor the digestion of starchy foods by ptyalin. The action of ptyalin is, on the contrary, unfavorably influenced by alcohol in 10 per cent. strength and, more particularly, by the acids contained in malt beverages and wines.

On reaching the stomach, alcohol produces a sense of warmth, which is promptly followed, as absorption takes place, by a general feeling of well-being and restfulness. When present in the stomach in small amount only, alcohol has no marked effect on peptic digestion, and often distinctly augments the secretion of gastric juice, itself becoming thereby progressively more dilute. It acts both by stimulating directly the

gastric circulation and the secreting cells to greater activity, and probably also by a special secretory influence of the alcohol after its absorption. Since Spiro, Frouin and Moulinier observed that alcohol administered per rectum caused in the stomach a marked flow of abnormally acid gastric juice. Chittenden and Mendel showed, moreover, that the relative amounts of pepsin and hydrochloric acid in the gastric juice were both increased. Thus alcohol in small quantities tends to hasten gastric digestion. Fatty substances being dissolved by it, their absorption is facilitated. The appetite, when poor, is improved.

When 5 to 10 per cent. of alcohol is present, peptic digestion takes place less rapidly than normal, the degree of interference varying with the kind of food to be acted upon. According to Klemperer and Battelli, however, gastric motility is hastened by moderate amounts of alcohol, while Bandl, Scanzoni and others have shown that liquids containing alcohol are much more rapidly absorbed from the stomach than liquids free of it. It thus happens in many cases that the interference of the alcohol with peptic digestion is more than counterbalanced by the hastened absorption as well as by the increased amount of gastric juice. Gluzinsky's experiments indicate that alcohol slows gastric digestion only during the period before its absorption; it then causes increased rapidity of digestion because of the special stimulating effect on secreting structures already mentioned. According to this author 60 Gm. (about 2 fluidounces) of cognac, taken during or before a meal, slows the digestion of carbohydrates and hastens that of meats, but when taken after the meal hinders both. It has been noticed that

spirits are much less potent in hampering peptic activity than are wines and especially malt liquors. In small quantities they distinctly aid digestion.

Using the method first devised by Cannon, the writer studied experimentally the effect of alcohol on the rate of discharge from the stomach in the Laboratory of Physiology in the Harvard Medical School. A relatively small amount of alcohol mixed with the food administered to the animals had distinctly an accelerating effect on the rate of gastric discharge and produced a higher maximum than the normal. The gastric peristaltic waves were deep and vigorous, and in most cases at the end of 3 hours no residue remained in the stomach. Contrary to these results in the third set of experiments where the 95 per cent. alcohol was used there was a slow initial discharge and a gradual rise to a maximum at the end of 3 or 4 hours. When at all evident the peristaltic waves were shallow and feeble and in some of the animals there was present at the end of 4 hours a considerable amount of food. L. T. Wright (Boston Med. and Surg. Jour., Nov. 2, 1916).

Alcohol passes quickly from the stomach into the intestines. Here also it is absorbed, and exerts, when in small amount, an effect similar to that produced on the stomach, viz., stimulates the mucous and other glands to increased activity. Relaxation of the bowels and meteorism are frequently influenced by it. *In vitro* alcohol in 3 per cent. strength, however, slows the digestion of proteids by the pancreatic juice (Chittenden and Mendel).

Nervous System.—When the action of alcohol has been exerted long enough, it acts as a depressant to the nervous system. The effects seen at first suggest primary cerebral stimulation, but it is a question whether these

phenomena are not really the result of impaired inhibition, in which case alcohol might be said to act as a depressant from the beginning. Small amounts of alcohol do, indeed, produce effects suggesting loss of inhibitory control over cerebral activities, though it must be admitted that the actual physiological existence of such a controlling function has not yet been definitely proved. In the primary stage of apparent excitation, the subject exhibits loss of control, as manifested by loose speech, laughter upon slight provocation, outbursts of the passions and exaggerated movements. The subject becomes selfish, irresponsible, and lacks will-power. Bunge, Schmiedeberg and others believe that these phenomena occur because the normal inhibitory influence on the cortical centers has been reduced.

> Alcoholism may be assumed, the writer concludes, when besides the lesions of chromatolysis in the third layer of large pyramidal cells of the brain, there is dilatation or congestion of the capillaries, thickening of the meninges, without leucocyte infiltration, and small hemorrhages. Jones (Prensa Med. Argentina, Sept. 30, 1918).

As an argument against the theory of primary stimulation it is pointed out that a primary stage of excitement is usually not seen when the subject remains in quiet and dark surroundings after taking alcohol, while certain individuals show no evidences of stimulation under any circumstances, but soon pass into a state of cerebral depression. Other observers believe that the physical excitement and the unusual flow of ideas and powers of speech often observed under the influence of alcohol indicate a primary stimulating effect on the same centers. The ability to perform muscular work has usually been found in experiments to be increased for a brief period by alcohol in small amounts, especially where fatigue exists, but this is very promptly followed by a distinct decrease; further, it is not proven that the preliminary increase is due to excitation of the motor areas, since the nerves or muscles themselves may instead have been affected. Kraepelin concluded from his experiments that motor activities were heightened by alcohol in small amounts and depressed by larger quantities, but that the mental activities were lowered for a period of twelve to twenty-four hours by it even in small doses. Alcohol acts also on certain sensory centers, reducing pain.

> Marchiafava was the first to call attention to primary degeneration of the nerve fibers in the corpus callosum and commissure in men with alcoholic psychoses. The clinical picture in this condition is that of a gradually developing feeblemindedness, with perversion or deadening of the moral sense; there may also be tremor and disturbances in speech, etc. Guizzetti (Riforma Medica, Apr. 24, 1915).

> Blix's test of the orientation capacity of the hand as a means of determining the amount of disturbance induced by small amounts of alcohol was applied by the writer. The test amount of alcohol was always 5 c.c., taken before rising, and the exercise was done 50 minutes later. There was always a falling off of from 20 to 50 per cent. when the alcohol was taken. C. Gyllenswärd (Upsala Läkareförenings Forhandlingar, 22, No. 3, 1917).

> In order to test the mental effects of alcohol, dotting machines were used for "attention" and lists of related words for "memory." It was found that the general effects of alcohol were to deteriorate these powers except under certain fatigue conditions, when alcohol improved both powers; opium, on the contrary, im-

proved both powers, whether under normal or fatigue conditions. The fatigue was engendered by loss of sleep for 3 nights. The tests were made every day. The more dilute the alcohol, the weaker the effect; alcohol taken after a meal had a much less evident result than when taken 4 or 5 hours after a meal. Smith and McDougall (Trans. Brit. Assoc. Adv. of Sci.; Med. Rec., Oct. 2, 1920).

After the initial stage of apparent stimulation, the actual depressant action of alcohol on the nervous system is no longer in doubt. Soldiers have been found to march better and remain stronger without alcohol than when supplied with it in moderate amounts. Large single doses produce signs of distinct brain depression, passing from muscular inco-ordination, with imperfect speech, impaired sensibility, and somnolence, to a state of unconsciousness similar to that of ether and chloroform anesthesia. The spinal cord is depressed by alcohol even before the unmistakable signs of cerebral depression occur, as shown by the early muscular inco-ordination (apart from disturbances of equilibrium) and diminished reflex irritability. The functions of the bulbar centers, however, are not markedly affected until late. On the peripheral nerves alcohol in large doses was found by Dogiel to exert a pronounced depressing effect in dogs. Motor nerves are believed to withstand this effect longer than sensory nerves. In the frog the response of the motor nerves to stimuli is at first increased when the vapor of alcohol is brought in contact with it, but the usual depressant action soon follows.

At the Nutrition Laboratory of the Carnegie Institution an exhaustive experimental study of the physiologic consequences of the ingestion of small doses of ethyl alcohol in man showed that it induced no facilitation of the motor processes, but that the depression of the simplest forms in the finger and eye movements seemed to be one of the most characteristic effects of alcohol. It is exactly these effects which were found to harmonize most closely with the average of all the effects for the several subjects studied. F. G. Benedict (Jour. Amer. Med. Assoc., Apr. 29, 1916).

Circulation.—Although the pulse-rate is commonly increased after the use of alcohol in considerable amount, Jacquet believes that where the subject can be kept free from external exciting influences, no such change in the heart-action is produced. The results of experiments intended to develop the action of alcohol on the heart have been contradictory. It is thought by many that the mammalian heart is slightly stimulated by alcohol unless given in large amounts, when it is depressed (Dixon and Bachmann, Wood and Hoyt, Loeb, Bachen). Alcohol in 2 per cent. strength passed through the coronaries of a cat's heart does not cause arrest of cardiac activity (Loeb). Other experimenters conclude that alcohol causes no increase in the work performed by the heart. According to Cushny the preliminary action of alcohol is to weaken the heartbeats. As for the blood-pressure, moderate doses have usually not been found to alter it. The advocates of primary cardiac stimulation by alcohol account for this by the dilatation of the peripheral blood-channels, which is often manifest in the flushed face, injected conjunctivæ, and heated skin surfaces observed after the use of alcohol. The speed with which the blood courses through the vessels is thereby increased (Hemmeter, Wood and Hoyt). Whether the vascular dilatation is due to an action

on the vasomotor centers or on the vessels themselves has not as yet been determined. The results include disturbances in the cerebral circulation; the brain may be the seat either of marked hyperemia or of anemia (Claude Bernard). Certain experimenters have at times observed increased blood-pressure due to alcohol; thus Kochmann noted in man a rise in the pressure upon the exhibition of 5 to 10 c.c. (1¼ to 2½ drams) of absolute alcohol. Such an elevation of pressure might be due either to a direct stimulating effect on the vasomotor centers, or, as many believe, to a reflex effect on these centers due to irritation of the gastrointestinal mucous membranes.

Report concerning a series of manometric blood-pressure tracings showing the effect of alcohol on dogs. By mouth it caused a marked rise in blood-pressure, with increased amplitude and a constant, or slightly slowed rhythm of heart beat. This rise gradually passed off in 5 or 10 minutes. By whatever method administered, alcohol, circulating in the blood, causes a gradual, progressive lowering of blood-pressure with decrease in amplitude but increase in rate of heartbeat. Clyde Brooks (Jour. Amer. Med. Assoc., July 30, 1910).

Though whisky raises for a few moments the systolic blood-pressure, it decreases secondarily cardiac efficiency, raises disproportionately the diastolic pressure, and lowers the pulse pressure. C. C. Lieb (Jour. Amer. Med. Assoc., Mar. 13, 1915).

The writer found experimentally that when alcohol is given orally to an unanesthetized animal there is a rapid rise in blood-pressure and respiratory rate and an immediate return to normal. This is due to local action. Given intravenously, gradually, in quantities sufficient to kill in 1 or 2 hours, no effect occurs until just before death, when a rapid fall of pressure takes place. When given through a stomach tube there is no effect. When it is given intravenously without excitement in the normal dog, no stimulation of the heart or respiration can be observed. Hyatt (Jour. Laborat. and Clin. Med., Oct., 1919).

Excessive amounts of alcohol cause a pronounced fall in the blood-pressure, since they depress both the heart and the vasomotor center. They have also been observed in animals to slow the heart action, and even produce cardiac arrest, in much the same manner as does chloroform. According to Pouchet, the secondary fall of blood-pressure is due largely to stimulation of the inhibitory pneumogastric centers; the pressure may, indeed, at a certain stage of the poisoning be brought almost back to normal by section of the vagi.

The ingestion of alcoholic beverages, even in small amounts, during or just after work, in which calcium cyanamide is used, induces special symptoms illustrated in the following typical case: An emphysematous worker, aged 55, who was occupied in breaking up cyanamide, took 0.3 liter of red wine at 11:25 a. m. In 3 minutes the pulse rate rose from 69 to 104, the blood-pressure fell from 160 to 110, and the rate of breathing rose from 16 to 22. Already in the second minute there was excessive vasodilatation of the face and conjunctivæ, marked pulsation of the temporals, then nausea; the man was compelled to stay recumbent, becoming faint as soon as he attempted to rise. The pressure remained 110 for an hour, then rose slowly. The signs of vasodilatation passed off in about an hour. The sensitiveness to alcohol from working with cyanamide lasts over 18 hours after cessation of work, though diminishing during this period: it then disappears completely, even in individuals who have long been working in the factory. J. P. Langlois

Blood.—Large amounts of alcohol must be present to cause perceptible changes in the blood in a short space of time. Foguet claimed to have ascertained that intoxicating doses, taken daily, were without effect. Pouchet states, however, that under small, repeated doses, the blood gradually undergoes fatty changes, owing to the fact that the emulsified fats entering the blood with the chyle are not consumed as normally.

> A research on the cholesterol and lecithin content of the blood of dogs kept under the action of alcohol, showed that besides the unusually high content of the blood in these bodies, the neutral fat of the blood is also increased. There seems to be an actual mobilization of the lipoids, a lipoidolysis, perhaps the expression of a defensive function. Ducceschi (Prensa Med. Argentina, Oct. 10, 1918).

In addition to the above changes the alkalinity of the blood is lowered, the coagulability rises, and a process of dehydration goes on, as shown by diuresis and increased secretions generally, whereby the blood becomes relatively more concentrated, the erythrocyte count and hemoglobin percentage rising. Schmiedeberg found that blood containing alcohol loses in part its oxygenating power,—a fact of considerable practical significance. *In vitro,* alcohol added to blood darkens its color, coagulates it, and causes hemoglobin to leave the erythrocytes. Such effects can only be obtained in the animal organism by the intravenous injection of alcohol in large doses. Under these conditions the red cells undergo marked changes in shape and color (Hayem). The fats and lecithin are dissolved, and the hemoglobin becomes dissociated from the stroma and precipitated in reddish, refractile droplets. Bordet and Massart showed alcohol to have a strong negative chemotactic influence on the white blood-cells, even when greatly diluted.

> Microscopic changes in the tissues as a result of alcohol, taken from observations on animals: 1. The most marked effects are produced on the blood-vessels. 2. The cells which line the vessels are swollen and broken, and there are serious retrograde changes in all of the tissues. The white blood-cells become swollen and necrotic. 3. The lymph-spaces become choked with broken-down white blood-cells, and the small blood-vessels are also completely blocked by plugs in detritus and dead tissue. 4. In the veins the blocking is often so severe that the vessels burst from the backing up of blood in them. The changes are always more marked in the vessels of the brain than elsewhere because they do not possess the special nerves which control their caliber, as do the vessels of other parts of the body. H. J. Berkley (Johns Hopkins Hosp. Bull.; Amer. Jour. of Physiol. Therap., May, 1910).

Respiration.—Volumetric estimations made before and after the ingestion of alcohol have shown fairly conclusively that, even in the absence of motor excitement, the drug causes an increase in the amount of air breathed. Usually the augmentation is more pronounced in fatigued or exhausted individuals. Considerable experimentation has been indulged in for the purpose of ascertaining whether the drug stimulates directly the respiratory centers in the medulla or whether the effect is of indirect origin, viz., through irritation of the gastric mucosa. Thus Loewy conducted experiments in which the irritability of the centers of respiration before and after the use of alcohol

was ascertained through its response to an increase of carbon dioxide in the blood. The results of these and other researches have not been entirely conclusive, but, in a general way, they tend to show that alcohol exerts, in man at least, little if any direct central stimulation, and therefore, that the improvement in respiration observed under the influence of therapeutic doses of alcohol is probably due to a reflex effect on the centers. An additional argument in favor of the latter view is in the fact that respiratory depression occurs only under exceedingly large doses of alcohol and at a late stage in the poisoning, tending to show that the effect of this drug on the respiratory centers is, under ordinary circumstances, not a very marked one. Yet it is well known that in the final stage of acute alcoholic poisoning the breathing becomes more and more shallow and infrequent, complete arrest ultimately occurring.

In fever, both the respiration and the heart-rate are slowed by alcohol. This seems reasonably accounted for by a lessening of general bodily excitement through the narcotic action of alcohol, without implicating a direct depressing action of moderate doses of it upon both the respiratory centers and heart.

Secretions.—Many of the secretions are to a certain extent activated by alcohol. The saliva and digestive secretions are increased reflexly by the local action of alcohol on the mucous membranes, as well as, probably, after its absorption, through direct contact of alcohol with the gland-cells as the drug circulates with the blood-stream. The sweat secretion is increased owing to the peripheral vasodilatation. The urine is also augmented. The question whether a direct exciting action on the renal epithelium is exerted or not has not

yet been settled, though the fact that albuminuria may result from excessive doses would seem to point to an irritative effect on the kidney cells.

Temperature.—Alcohol in ordinary doses causes a slight fall in the body temperature ($\frac{1}{4}°$ to $1°$ C., according to Cushny), owing to the dilatation of the superficial blood-vessels, which exposes a larger amount of blood to the cooling influence of the surrounding air. At the same time a sensation of warmth is experienced, and the temperature of the skin may rise considerably owing to its flushed condition. If a large amount of alcohol be taken the fall of internal temperature may be exaggerated owing to the complete motor inactivity. The same will occur under a moderate dose of alcohol if the subject be subsequently exposed to cold.

Metabolism.—Alcohol causes but little change in the oxygen intake and carbon dioxide output, which, after its ingestion, show no modification beyond that to be expected from any other substance yielding energy to the system by oxidation. Of course, if alcohol be taken in amounts sufficient to produce sleep, the respiratory gaseous interchanges will be lowered because of the muscular inactivity. Where the drug is taken repeatedly in moderation, however, a gradual increase in the oxidizing power of the blood occurs, apparently corresponding in amount to the degree to which tolerance of alcohol has been developed in the individual. This fact was well illustrated in the experiments of Hunt on the toxicity of methyl cyanide, a compound whose poisonous effect is proportional to the extent to which it is oxidized to hydrocyanic acid in the system. Animals given repeated small doses of alcohol, insufficient in themselves to elicit signs of intoxication,

showed an increased susceptibility to methyl cyanide, demonstrating that the oxidizing power of the blood had become greater.

> The effect of alcohol on respiration was studied by the writer on recumbent and breakfastless men. From 30 to 45 c.c. (1 to 1½ ounces) of ethyl alcohol (suitably diluted) were given. The respiration rate was not appreciably affected by alcohol nor was the type of respiration changed, unless there was restlessness. The heat production, as indicated by the oxygen consumption, was ordinarily unchanged; in about one-fifth of the experiments there was a rise in heat production of from 5 to 7 per cent. It diminished the volume of air breathed per minute in most instances. Higgins (Jour. Pharm. and Exper. Therap., May, 1917).

In addition, the administration of alcohol, which is almost entirely destroyed in the system by oxidation, naturally tends to preserve from combustion other oxidizable substances present—fats in particular. This accounts for the well-known fattening tendency of alcoholic beverages, when habitually taken in any but very moderate amounts (see section on Alcohol in Nutrition).

Immunity.—As to the influence of alcohol on the powers of resistance of the individual to disease, it is well known that alcoholics are less resistant to acute infections and more susceptible to dangerous shock from bodily injury than are the temperate. Likewise, animals given alcohol and subsequently inoculated with pathogenic organisms or injected with disease toxins have always shown a low degree of resistance as compared to normal animals. Deléarde and Laitinen in their experiments found it "almost impossible to confer immunity against rabies, tetanus, and anthrax on alcoholized animals." The question, however, whether alcohol in the amounts in which it has been used in the treatment of acute febrile diseases in non-alcoholics has a similar prejudicial effect has not been definitely settled.

[Inasmuch as the defensive power of the body fluctuates with its vital activity, beverages rich in alcohol, besides inhibiting the life process itself, place it at the mercy of disease-breeding germs, and thus actually help to destroy life through deoxidizing or reducing action on the blood.

This is further emphasized by the influence of alcohol on the ductless glands themselves. While small doses or weak solutions, as stated by Lorand, stimulate these organs, large quantities of beverages strong in alcohol cause their degeneration, as shown by numerous autopsies. My work on the "Internal Secretions" contains a microphotograph showing a pituitary body in which alcohol produced sclerosis. Hertoghe and de Quervain have found alcohol harmful to the thyroid—an organ which, as is well shown by cretinism and the marvelous effects of thyroid preparations in this disease, has much to do with the development of the body. The defensive functions of the body, if carried on, as I hold, by the ductless glands, are thus directly hampered by the use of alcohol in any but very weak solutions. This coincides with the recent observations of Parkinson, who studied the influence of alcohol on the autoprotective functions of the body. While his experiments showed that small quantities temporarily enhanced the production of antibodies, as soon as they were replaced by large doses the opsonic index fell; and if their use was continued, it remained low permanently, which meant that the immunizing functions were paralyzed. This confirmed the earlier experiments of Müller, Wirgin, and others referred to below.

It is because of this fact that drunkards in general fare so badly in infectious diseases; their autoprotective mechanism is powerless to defend them. Quite in accord with these teachings of experience, Parkinson found that the reaction to vaccines was much less effective in alcoholized rab-

bits than in normal rabbits, and that the difference was still more marked when living micro-organisms were used. Many experiments by competent observers afford evidence in the same direction. Again, I have shown that the immunizing process of the body is closely linked and runs on parallel lines with oxidation; since alcohol in anything but small doses reduces oxidation, it inhibits in proportion our power to fight disease during the active or defensive phase of the morbid process, especially in febrile infections and toxemias.

If alcohol is used at all, therefore, in the acute infections and toxemias, it should only be given in small quantities and freely diluted. But better agents to enhance the defensive process are now available. C. E. DE M. S.]

Friedberger, Müller, Wirgin, and other observers found that, in rabbits, the administration of alcohol for some days in amounts sufficient to produce a mild degree of intoxication interferes with the formation of antibodies in the blood. The greater the time allowed to elapse, however, between the injection of the antigen and the giving of alcohol, the less the restraining effect of the latter on the development of protective substances. Experiments conducted by Laitinen, in which animals were given for some time doses of alcohol so small as to correspond with the amounts taken dietetically by moderate users of alcohol, did not reveal any pronounced disadvantage in the habitual use of small quantities of alcohol as regards susceptibility to disease, the mortality being but slightly greater than among the animals not given alcohol.

Ingestion of alcohol is quickly accompanied by a lowered opsonic index, but the index as quickly returns to the normal with cessation of the alcohol. The amount needed to bring about this result had no influence on the resistance of the animal to infection. Abbott and Gildersleeve (Univ. of Penna. Med. Bull., June, 1910).

Study of protein metabolism and utilization, and especially the partition of nitrogen in the urine, under the influence of alcohol, carried out on man and dogs under fixed and comparable conditions of diet. There is no pronounced disturbance in the alimentary utilization of the foodstuffs. Moderate doses exert a protein-sparing action, which is succeeded by loss of nitrogen when larger quantities of alcohol are administered. The partition of urinary nitrogen remains remarkably unaltered, with the exception of an increased elimination of ammonia nitrogen and a higher output of purins. The most significant impression afforded was the absence of pronounced alterations indicative of markedly disturbed protein metabolism, even when comparatively large doses were continued for days and weeks. Mendel and Hilditch (Amer. Jour. of Physiol., Nov., 1910).

[As is the case with all food accessories, coffee, tea, pepper, common salt, etc., alcohol becomes toxic when used immoderately, and when insufficiently diluted. Light wines, beer, and other beverages that contain a very small proportion of alcohol, when taken in moderation, tend to activate the functions of the ductless glands, and, therefore, the autoprotective functions of the body. The harmful influence of alcohol begins as soon as the proportion of absolute alcohol in a beverage exceeds 5 per cent. to any marked degree, the toxic effects being due mainly to its property of becoming oxidized at the expense of the blood and other body fluids and cellular elements. When the proportion exceeds 10 per cent. and approximates that of brandy, whisky, and many patent or proprietary nostrums, alcohol becomes an active toxic; it tends to paralyze the functions of the ductless glands, and, therefore, the autoprotective functions, thus giving free sway to pathogenic germs, their toxins and other toxics, venoms, toxic wastes, etc., that may be present in the blood, thus defeating indirectly and insidiously the efforts of the physician. C. E. DE M. S.]

The study of necropsies at the Boston City Hospital on cases dying from alcoholism during the 15 years previous to 1915, shows that the great majority of alcoholics show no change except an abundance of fat in the liver cells. The writer found that 30 investigators gave ethyl alcohol to animals, and of these 17 produced no lesions in the liver, while 13 claimed to have produced cirrhosis; those that produced cirrhosis worked with rabbits. To clear up this question the writer gave alcohol persistently to 125 animals, including guinea-pigs, cats, rabbits and dogs, and in no instance could any lesions, however slight, be produced. Other substances than alcohol were also given to a series of 75 animals, with essentially negative results. The writer believes that the so-called alcoholic cirrhosis is not produced by alcohol, and that the liver is not injured by the alcohol carried to it by the blood or lymph. F. A. McJunkin (Arch. Internal Med., May, 1917).

Absorption and Elimination.—The absorption of alcohol is very rapid, unless it be so concentrated as to coagulate the albumins with which it comes in contact. Roughly, 20 per cent. of alcohol ingested is absorbed from the stomach, and the remaining 80 per cent. from the intestine. Proceeding to the liver with the portal blood, it is in part arrested in this organ, the other portion passing through to enter the general blood-stream. Eventually much of the latter portion leaves the capillaries by exosmosis and is absorbed by the various tissues. The liver and brain have a special affinity for alcohol, the former fixing four times and the latter twice as much as is present in the blood (Pouchet). More than 98 per cent. of the whole amount ingested is oxidized in the tissues (Atwater). The remainder passes out with the urine unaltered, though traces may still remain in the blood after the first twenty-four hours. The aroma of the breath of alcohol users is due rather to higher alcohols and by-products eliminated in this manner than to ethyl alcohol (Cushny). According to Brauer, some alcohol is excreted with the bile, then reabsorbed from the intestinal tract. An insignificant amount may leave the body with the sweat and milk. The products of the oxidation of alcohol in the system are believed to be acetic acid, carbon dioxide, and water. According to the researches of Dujardin-Beaumetz and Jaillet, it is oxidized in the red cells themselves, with the formation first of acetates of the alkali metals, then of carbonates. When the oxidizing capacity of the blood-cells is exhausted alcohol begins to be eliminated in large amount with the emunctories and to accumulate in the tissues.

Rôle of Alcohol in Nutrition.—The painstaking experiments of Neumann, of Atwater and Benedict, and of Rosemann have shown alcohol to be capable of sparing the fats and carbohydrates of the body through its combustion in their stead, i.e., where the amounts of fat and carbohydrates ingested are insufficient for the needs of the body alcohol will, to a certain extent, act as a substitute, and prevent the remaining reserve of these substances in the system from being exhausted. The combustion of alcohol, however, yields but a comparatively small amount of heat, the body temperature being, therefore, seldom raised by it, but rather lowered, owing to the peripheral vasodilatation it also produces, with the consequent increase in heat loss. Neumann concluded from his experiments that alcohol could take the place of a chemically equivalent quantity of fat in the diet, and also that alcohol given in combina-

tion with a diet in itself sufficient would bring about an economy of proteins—as measured by the nitrogen excretion in the urine—in the same way that an extra amount of fat would. When moderate amounts of alcohol are taken, the first result is an increase in the amount of nitrogen excreted, which persists, as in the case of any other change in the non-nitrogenous constituents of the food, until the organism has become used to the new diet, *i.e.,* through a period of three or four days. After this the protein-saving property of alcohol asserts itself, the amount of urea and uric acid, as well as of sulphates and phosphates, eliminated with the urine showing a decrease. According to Pouchet, however, the proteins are spared by alcohol only if the subject is receiving in the diet an amount of protein in excess of the needs of the body at the time. If not, or in any case if the administration of alcohol be long enough continued, the amount of nitrogenous wastes will soon show an increase until the utilization of the body proteins becomes greater than normally—a condition of affairs unfavorable to the nutrition of the body. The same result will obtain at once where excessive, instead of moderate, doses of alcohol are used, the drug acting as a spur to the breaking down of the albumins.

The advantages of alcohol as a source of body energy may be said to lie in its ready absorption, the fact that no digestion of it is required, and that it is easily oxidized. In fever or conditions of central nervous exhaustion, with resulting temporary digestive failure, alcohol is, therefore, available for cautious use as a food. Roughly speaking, 4 minims of alcohol will yield the same amount of energy as 7 grains of

sugar, starch, or protein or 3 grains of fat (Committee of Fifty, 1893).

The disadvantages of alcohol are that it has toxic side effects, that it leads to obesity, and, probably, that, even in the temperate, it tends to lower the resisting power of the body to disease.

[Alcohol is considered as a food-sparing agent by some observers, its value corresponding with its dynamic equivalent of pure food hydrocarbon. This presupposes, however, that alcohol is utilized by the tissues in the same manner as these hydrocarbons—merely because its oxidation liberates energy in the form of heat. But this is a fallacious conception; alcohol only simulates normal oxidations; far from being the product of cellular exchanges which constitute the vital process, the heat it liberates is at the expense of the tissue, since by becoming oxidized itself, especially in the liver—whereby the body is protected against its toxic effects —it utilizes oxygen intended to sustain tissue metabolism. If alcohol were a food, large doses would prove more profitable to the organism than small ones; but the reverse is the case; large doses inhibit all activities that would be enhanced by a liberal use of food. The debilitating action of alcohol on the nervous system, for example, has been demonstrated by Bunge, Schmiedeberg, Ach and Krepelin, and others, while Dogiel found that it depressed markedly both motor and sensory nerve-centers. It does this not only with nervous tissue, but with all tissues. A depressing agent cannot logically be regarded as a food. C. E. DE M. S.]

In healthy persons alcohol unquestionably plays the same rôle as a food, *e.g.,* a carbohydrate or a fat. In contrast to fats and carbohydrates, alcohol spares the proteids only in those cases in which the organism has become accustomed to the action of the stimulant, which usually takes several days. In disease alcohol apparently acts upon metabolism in the same way as in health. It is particularly useful as a food in diabetes mellitus; by taking the place of fats in the food it lessens the production of

the acetone bodies. Hare showed that alcohol raises the power of the blood to destroy bacteria. Friedberger found that under the influence of alcohol the blood acquired an increased resistance against the cholera vibrio. Mircoli found that under the influence of alcohol the body acquired the power to resist the tubercle bacillus. A. K. Sievert (Roussky Vratch, Oct. 24, 1909; N. Y. Med. Jour., Jan. 1, 1910).

[The protective influence of alcohol referred to here applies to small quantities only. Everyone knows and hospital experience has amply and conclusively shown that alcoholism greatly weakens the power of the body to resist disease. C. E. DE M. S.]

Industrial fatigue, *i.e.*, a diminished capacity for doing work relative to the taking of alcohol was studied by the writer. He concludes that alcohol has little immediate effect upon the physical side of fatigue, whatever its ultimate effect may be. The amount of output is perhaps increased to a small extent for a short time, but the increase soon falls off and is replaced by a diminution. The influence of alcohol in the psychical side of fatigue was more profound. It led immediately to a feeling of renewed vigor and increased strength. But here also the effect was transitory. A. F. Stanley Kent (Lancet, July 28, 1917).

External Action.—Applied to the skin and allowed to evaporate, alcohol reduces the local temperature because of its marked volatility. It may also exert an anesthetic effect. If evaporation be prevented, however, and the contact maintained for some time, alcohol acts as an irritant. Owing to its rather high diffusion power, it penetrates through the cuticle to the underlying tissues, and induces a sensation of heat, often preceded by itching and accompanied by reddening of the skin surface. It may thus be employed as a counter-irritant. For such effects a concentration of about 60 per cent. or over is required, more dilute solutions not giving rise to distinctly irritative phenomena. When applied to ulcers and other open surfaces, alcohol may, through its irritant properties, hasten tissue repair. The prominent local effects of concentrated alcohol include the abstraction of water from the tissues, and the coagulation of albumin. It is because of these effects, and also by dissolving out the fat, that alcohol hardens the skin when repeatedly applied. It is sometimes used to cover sores or wounds with a thin, protective, air-excluding layer of coagulated albumin, which facilitates healing. Alcohol may also act as an astringent, a property not infrequently availed of in such condition as salivation, pharyngeal relaxation, scurvy, etc., alcoholic preparations being employed as mouth-washes and gargles. The irritant and astringent powers of alcohol are naturally more pronounced upon the mucous membranes and upon wound surfaces than upon the skin, and dilute preparations can, therefore, be used on the former to procure effects such as only concentrated ones would produce on the skin. Inhalation of the vapors of alcohol is capable of causing temporary spasm of the laryngeal muscles through reflex irritation. Alcohol has noteworthy antiseptic and germicidal properties, which may be utilized in the disinfection of wounds. According to Harrington and Walker, 60 and 70 per cent. alcoholic solutions, applied to wounded surfaces for at least five minutes, are the most efficient in destroying bacteria. In these percentages alcohol corresponds in strength to about 3 per cent. phenol (Cushny). Dry bacteria may not be destroyed by a day's exposure to absolute alcohol.

THERAPEUTICS.—As a "Stimulant."—The opinion of the medical profession in regard to the value of alcohol as a stimulant is divided, and the extent to which the drug is employed in the treatment of disease (exception being made of its external uses) is on the decline.

The more recent studies have brought out the importance of the vasodilator influence of alcohol, and cast a shadow on its effectiveness as a true stimulant. By many it is believed that a part, if not all, of the stimulating effect of alcohol results from the local irritation produced by it in the stomach, the centers in the medulla oblongata being thereby excited reflexly.

[Buchner, Chittenden, Mendel, Jackson, and many other authorities have shown that beverages which contain a small proportion, about 5 per cent., of absolute alcohol, such as light wines, beer, etc., increased the production of gastric juice and the activity of the digestive process. Being entirely oxidized in the stomach and promptly eliminated by the lungs and kidneys, this small percentage, unless taken in large quantities, does not influence morbidly either the blood or its oxidizing body. Such is not the case, however, when the proportion of absolute alcohol exceeds 5 per cent. to any marked degree. A beverage containing 10 per cent., for example, retards digestion manifestly, and if stronger, as is the case with brandy, whisky, etc., it tends besides, as first shown by Claude Bernard, to cause coagulation of the gastric secretion and its ferments. Under these conditions, the functions of the digestive tract are not alone interfered with, but considerable alcohol is absorbed into the blood. It is this absorbed alcohol which does incalculable harm. Being oxidized at the expense of the blood's oxidizing body—of adrenal origin—it robs the tissues of that which sustains their life. C. E. DE M. S.]

Experience of many years has taught the writer that there are no harmful effects from the *strictly mod-*

erate (his italics) use of alcohol by persons of sound mental and physical health, such as British soldiers supposedly are. He agrees with Mercier and Lyon Smith that asylum statistics tend to show that insanity produces inebriety, and not *vice versa*, as is so frequently averred by the zealous champions of total abstinence. J. W. Astley Cooper (Lancet, Nov. 14, 1914).

Partly because of the fact that it is often the only remedial agent immediately available, it is still largely administered, especially by the laity, in all varieties of emergencies. Its effect, though of short duration, is exerted promptly.

No amount of whisky will lead to intoxication when its effect is needed to combat sepsis, and his cases of thorough sepsis relieved or cured by alcohol extend over more than half a century. Among these were cases of diphtheria with mixed infection where his experience had shown that no such infection was amenable to the action of antitoxin. A. Jacobi (Amer. Med., Sept., 1913).

At the Venice hospital connected with the medical school no harm resulted from the complete discarding of wine and brandy. The educational effect from the suspension of alcohol was excellent and widespread. Even the elderly chronic cases seemed to do just as well without it, and 78 per cent. assured the investigators that they did not feel the loss of the wine as a privation. The others seemed to miss it only as an agreeable relish. Jona (Policlinico, Nov. 11, 1917).

As a cardiac and respiratory stimulant alcohol is made use of in immediately dangerous conditions, such as **syncope, shock, collapse,** severe **hemorrhage, asphyxia,** and **poisoning by depressant drugs,** as well as, in many instances, in the course of acute infectious diseases, such as **typhoid fever, typhus, pneumonia, diphtheria,**

small-pox, scarlatina, septicemia, erysipelas, tetanus, yellow fever, cholera, dysentery, influenza, etc. The consensus of present opinion is that alcohol should never be administered continuously, even in severe infections, but should be reserved for periods of unusual depression, when special stimulation is necessary to tide the patient over a dangerous crisis. In selecting the dose to be used, the vasodilator influence of alcohol must always be remembered, excessive doses tending to lower markedly the tone of the blood-vessels,—the importance of which tone in the maintenance of cardiac activity is well recognized. According to many, indeed, the use of alcohol in shock is to be avoided, as this is a condition of paretic vasodilation, and the vasodilator effect of alcohol exerted after its absorption is likely to prove more harmful than its primary reflex stimulating effect on the heart and respiration will have done good. The same applies in severe hemorrhage.

> For each gram of alcohol oxidized in the body 7 large calories of heat are produced. Glucose, on the other hand, yields but 4.1 large calories of heat for each gram similarly consumed. Thus, alcohol, with no expenditure of digestive energy, and with the expenditure of less oxygen, yields a much larger production of heat and energy. It has great power for good when the system is in a pathological condition or greatly debilitated from any cause and cannot secure the necessary heat and energy from the ordinarily used food elements. Like food substances, alcohol is a stimulant, but, in addition, it can be oxidized in the body when sugar and fat cannot be so utilized. Many lives have been saved by the proper use of alcohol in times of dire need. No one has yet proved that alcohol cannot be used so as to

secure a stimulating effect without developing any of the subsequent depressing action. It would be a great mistake to drop so valuable an agent from the pharmacopeia. W. H. Porter (N. Y. Med. Jour., Apr. 3, 1920).

In emergency conditions, large doses of alcohol, e.g., 1 or 2 ounces (30 to 60 c.c.) of whisky or brandy, are not infrequently administered. Where, owing to unconsciousness or profound adynamia, the spirits cannot be swallowed, they may be injected subcutaneously. By this method absorption of the drug is more rapid, and its general effect correspondingly hastened. Alcohol may also be given by rectum, preferably as brandy.

In the treatment of **wounds** inflicted by **venomous snakes** and **poisonous fishes**, the internal use of alcohol has long been considered an effective measure, though the dea that the drug exerts a specific antidotal effect in these cases appears to be based on pure assumption. Large doses are customarily given in these cases, but this should certainly not be pushed to the point of adding an acute intoxication to the difficulties with which the system already has to contend.

In the prostration attending cases of **meat poisoning** or **ergotism**, the administration of alcohol also often proves valuable.

As a Vasodilator.—The value of alcohol in feverish or frankly febrile conditions depends in reality on not a single, but a group, of effects, which have been enumerated by Sollmann as follows: 1. Dilatation of the cutaneous vessels. 2. Counteraction of the nervous phenomena of fever, through narcotic action. 3. The furnishing of a readily absorbable food. 4. Diuresis. Among these effects peripheral vasodilation ranks as the most important.

When the pulse becomes of the high-tension variety, owing to excitation of the contractile vascular walls by disease toxins, and the superficial circulation becomes sluggish, for the same reason, alcohol is likely to prove beneficial by dilating the vessels, lowering the tension, facilitating the work of the heart, and promoting perspiration. It will act thus pre-eminently as a restorer of the circulatory equilibrium. Certain particular indications for the use of alcohol in fevers have been formulated, viz., where in addition to a frequent, small, or irregular pulse or respiratory depression there are present dryness of the tongue and skin, together with restlessness and delirium or, on the other hand, indifference and hebetude, and perhaps subsultus tendinum,—phenomena commonly grouped under the term "typhoid state." While, in a general way, the validity of these indications for alcohol seems to be established upon the basis of past experience, it cannot be said that the drug will invariably be productive of benefit where the indications are present. If, alcohol having been administered, the pulse and respiration are improved, the mouth and skin rendered moist, and the mental condition corrected, the propriety of employing it in the individual case will become apparent.

As a vasodilator in chronic high arterial tension alcohol should ordinarily not be used. This indication is present in arteriosclerosis and gout, and is a symptom and sign in late middle life or old age. If the condition requires treatment it is much better managed by nitroglycerin, thyroid extract, potassium iodide, or small doses of chloral. If arteriosclerosis is present and the patient is well along in life and is accustomed and has been accustomed to take alcohol regularly in doses that do not

intoxicate, it may be unwise to stop the vasodilating effects of the alcohol until it has been ascertained that some other treatment will be as conducive to his well-being. In other words, the physiological relief from high tension which he has been accustomed to acquire by taking alcohol cannot be abruptly stopped without due consideration of the consequences of withdrawing the drug. (Jour. Amer. Med. Assoc., Nov. 6, 1909).

The dose of alcohol given in the **febrile diseases** has usually been that represented by $\frac{1}{2}$ to 1 ounce (15 to 30 c.c.) of whisky or brandy, diluted with water, this amount being repeated every two to four hours. While it has been a matter of common observation that very large doses of alcohol may be given in fever without eliciting the ordinary signs of intoxication, this fact should not be interpreted as giving the physician license to introduce alcohol into the systems of patients without due consideration of the dosage. It should be kept in mind that alcohol, though setting free energy in the form of heat through its oxidation, in doing so draws upon the supply of oxygen present in the tissues, and if caused to accumulate in the system through injudicious dosage is likely seriously to interfere with other oxidative processes essential to the welfare of the economy. Hence the tendency recently has been, if alcohol is used at all in fever, to limit strictly the amount given to what is necessary for amelioration of the symptoms.

According to Osborne, a dose larger than 1 to 3 teaspoonfuls, once every three hours, is probably never indicated in febrile conditions; if this dosage be exceeded, the harmful effects resulting when alcohol is given in amounts that overtax the oxidizing powers of the

tissues and lead to accumulation of the drug in the system will be avoided. Butler counsels that, even in cases where alcohol proves beneficial, it should rarely be given throughout the twenty-four hours, but reserved for periods when the heart action grows especially weak, usually in the interval between midnight and 7 A.M. One fluid-ounce (30 c.c.) of whisky may be given before midnight and repeated every three hours. In lieu of pure whisky or brandy, diluted alcohol may also be advantageously given in the form of milk punch or eggnog.

Alcohol is frequently used to increase the warmth of the body surface in the presence of chilly sensations or after exposure to cold. This is accomplished through the peripheral vasodilation which it produces. It must not be forgotten, in this connection, that peripheral vasodilation results in increased heat loss; if, *during* exposure to cold, peripheral vasodilation be produced and maintained for some time, as by repeated ingestion of alcohol, the result cannot but be an excessive loss of body heat, with merely temporary relief, and ultimate lessening of the resisting powers. Hence alcohol to warm the body surface should only be given *after* exposure or just before the period of exposure is to terminate.

In the initial stage of colds and of acute catarrhal inflammations of the respiratory passages in general, alcoholic preparations have been much used with the idea that by sharply activating the circulation of blood at the periphery local congestions will be relieved and the cold thus aborted. The patient takes a good-sized dose of whisky, followed by smaller doses every three or four hours, and stays in bed for a day, to facilitate the re-establishment of the

circulatory equilibrium. While there is no doubt that alcohol, in combination with external warmth, will often bring about the desired result, the same effect can be procured by means of a hot bath, a coal-tar drug, and a saline purgative, without resorting to the use of alcohol.

In arteriosclerosis alcohol will act as a vasodilator and doubtless frequently performs this office in elderly individuals accustomed to its use, but it should never be prescribed as such by the physician.

Where the eruption is delayed in the acute exanthematous diseases, a dose of whisky, taken hot, may bring about its early appearance.

As a Narcotic and Hypnotic,—The slightly depressing action of moderate doses of alcohol on the cerebral functions is a contributing factor in its usefulness in febrile conditions. Mild delirium will be relieved by it, or if no delirium be present the oncoming of sleep will be favored. The narcotic action of alcohol, however, is only of secondary importance, and should not be utilized unless there are other indications for the use of the drug. In febrile states a part of the quieting effect on the brain is due to a lowering of the tension in the cerebral circulation through the general vasodilation which the drug produces.

In mild degrees of insomnia in the aged, a little alcohol taken before retiring will promote sleep. But it is preferable to use other remedies; thus where the insomnia, as is often the case, is due to high blood-pressure, nitroglycerin should be substituted for alcohol, as a vasodilator. A mixture of equal parts of hot milk and of good ale or beer has been recommended as a promoter of sleep.

Although alcohol in proper dose and in the proper form has an hypnotic effect not only by dilating the peripheral vessels and relieving the tension of the cerebral circulation, but also by its quieting effect on the nervous system, it should not frequently be considered or used as a **hypnotic.** Still, instances occur both in acute illness and in debilitated patients where it seems to be the safest and the most satisfactory of hypnotics. Of course, when alcohol is used thus as a drug it should be stopped by the physician as soon as he considers that the patient can tolerate another hypnotic, or that the positive indication has ceased to exist. In very old people who cannot sleep, alcohol as a "nightcap" has been frequently advised. Sleeplessness in senility is frequently due to high-tension circulation, and one can often cause these patients to sleep as well with small doses of nitroglycerin, administered at bedtime, as by alcohol so administered. (Jour. Amer. Med. Assoc., Nov. 6, 1909.)

Similarly, in insomnia in greatly weakened individuals, where alcohol may seem, for a time, the best hypnotic to use, other drugs should be substituted for it as soon as the patient's general condition permits. Beer or well-diluted spirits are most effective where the hypnotic action of alcohol is desired.

In **neuralgia** as well as **melancholia** and other forms of mental distress alcohol has given relief through its narcotic effect, but the danger of inducing chronic alcoholism in these cases is such that it is questionable whether it should ever be employed.

As a Stomachic, Antemetic, etc.— Ingested before or during meals, alcoholic preparations will frequently exert a pronounced beneficial effect in cases of **atonic dyspepsia** or in **anorexia** or poor digestion due to physical or mental **fatigue, acute illness,** etc. A small amount of wine or beer, or a little brandy diluted with water, by exerting a mild stimulating effect locally improves the gastric circulation and thereby promotes the secretory activity where this is deficient. The psychic effect of the odor and taste of wine, when agreeable to the patient, probably also plays a not inconsiderable part in improving the appetite. Dry wines should be given the preference in these cases, the sugar of sweet wines being detrimental. Where anorexia is very marked, bitter tonics, such as calumba or quassia, in the form of tinctures or gentian or cinchona, in the compound mixtures, may be given in addition.

In certain forms of indigestion, alcohol does more harm than good, *e.g.,* where there is hyperacidity, or where the gastric mucosa is acutely inflamed. In all cases, moreover, where the necessity for gastric stimulation is likely to persist, *e.g.,* in the chronically debilitated and in the neurotic, the use of alcohol as a stomachic and stimulant to digestion is to be entered upon only with extreme caution, lest chronic alcoholism be the final result. This danger is less to be feared in the aged than it is in the young or middle-aged.

In **vomiting,** *e.g.,* in **seasickness** and in the **vomiting of pregnancy,** alcohol, especially in the form of champagne, sometimes proves helpful. A little brandy may be given on cracked ice in these disturbances, but champagne is decidedly the most effective preparation, combining the local anesthetic property of alcohol with the sedative action of carbon dioxide gas. In a somewhat similar manner, the **pain resulting from flatulence,** as well as **gastralgia,** may be relieved by the use of brandy (Butler).

In **diarrhea,** brandy is generally believed to exert a favorable influence,

though the reason for its beneficial effect is not known. Red wines, by virtue of their tannin content, also tend to counteract diarrhea,—especially Bordeaux, dark Burgundy, and currant wine.

In conditions of **general debility** and during **convalescence** from exhausting diseases, even in the absence of gastric symptoms, alcoholic preparations are frequently given as general stimulants and reconstructives. The benefit produced results in part, doubtless, from activation of the digestive processes, but the food value of the preparations used, generally rich red wines, such as port and Madeira, or else beer, ale, porter, brown stout, and malt extracts, because of the additional nutritive substances they contain, must also be given due credit. To these favorable influences may be added the tendency to sleep and rest as a result of the narcotic action of alcohol, the improved distribution of blood through peripheral vasodilatation, the lessened resistance to cardiac action offered by the vessels, and the euphoria of the primary stage of alcoholic action. In severe cases of **diabetes mellitus** alcohol has also been used as a food.

> Use of alcohol as a food in cases of severe **diabetes**. For years its value in such cases has been known clinically. But until recently we did not know whether the action was pharmacological or whether it was nutritive. In 1906, Benedict and Török, in studying the origin of acetone bodies in diabetes, substituted the fat of the dietary by alcohol and found a marked decrease in the output of acetone, sugar, and nitrogen. The sugar alone decreased 18 per cent. In severe cases with high ammonia the output was greatly decreased. Their work added further evidence of the protein-sparing action of alcohol. Neubauer, simultaneously, found alcohol of great service in severe diabetes. He used a wine containing

10 per cent. alcohol, allowing daily 12 to 24 ounces, equivalent to 450 to 900 calories of energy. He found regularly in severe cases a marked reduction in the output of sugar, acetone, oxybutyric acid, and ammonia. The total nitrogen and the amount of urine were decreased. In light cases of this disease, alcohol was of much less importance, but in severe diabetes, where the tissues cannot utilize carbohydrates, where only a little or no fat is allowable, and where protein alone tends to aggravate the conditions, alcohol finds an invaluable place in the dietary. Aside from its action in diabetes and a few conditions of malnutrition, there has been no evidence produced thus far that alcohol is a better food than the sugars and starches. There is some reason to believe it somewhat inferior to them. There is abundant evidence that, on account of its habit-producing power and its baneful effects when used in excess, it should be condemned as food for healthy, normal individuals. Scarbrough (Yale Med. Jour., Feb., 1910).

As a Diuretic.—Dilute gin, light acid white wines, and light beers are the most strongly diuretic preparations of alcohol. This property can, however, only be considered as a relatively unimportant adjunct to the other actions of alcohol.

In Phenol Poisoning.—The value of alcohol in phenol poisoning has been shown to be due to the ready solubility of the phenol in it, the local action of phenol in concentrated form being thereby hindered. It is to be observed that this very dilution of the phenol is likely to hasten its absorption into the general system. Hence after giving the alcohol—preferably dilute—the physician should see that the stomach is emptied as soon as practicable.

External Uses.—Applied locally, alcohol has antiseptic, anesthetic, cooling, stimulating, solvent, astringent, dehydrating, and hemostatic proper-

ties. It is, therefore, a valuable agent in the treatment of **wounds,** especially **infected wounds,** in the management of which whisky, undiluted or diluted in the proportion of 1 to 4 of water, may be employed with advantage. In **snake-bites** concentrated alcohol mixed with ammonia may be used as a lotion after the poison has been sucked out; it is similarly useful in insect stings. In **puerperal sepsis** 50 per cent. alcohol has been used as an intra-uterine douche, and in 25 to 50 per cent. strength as a packing; better agents are, however, at our disposal.

For the treatment of **sprains, inflamed joints, contusions, strained muscles and tendons, headache, neuritis, abscesses, slight burns, erythema,** and **erysipelas,** alcoholic evaporating lotions are extensively used. A lotion composed of alcohol 8 parts, ammonium chloride 1 part, vinegar or dilute acetic acid 4 parts, in water 64 parts, will be found generally serviceable. Where a greater degree of absorption is desired, a gauze pad may be moistened with alcohol, applied over the involved area, and covered with rubber tissue. In **phlegmonous inflammations,** Salzwedel cleanses the part with ether, applies thick layers of cotton saturated with 90 per cent. alcohol, and covers the whole with an impermeable material, perforated in such manner as to delay, but not entirely prevent, evaporation. By this plan, he states, fever is lowered and the suppurative process hastened. Similarly, in **sycosis, furunculosis, indolent ulcers, whitlow,** etc., Heuss employs compresses consisting of 6 to 8 folds of gauze wet with 95 per cent. alcohol and covered with an impermeable dressing. Kaiser employed alcohol dressings in 93 cases of various

inflammatory affections, and claimed very gratifying results; the distinctive feature of this method was that as a preliminary step, all fatty matter is removed from the involved area with benzine and alcohol (Bulkley).

Permanent applications of strong alcohol of great service in combating all **inflammatory conditions** in which there is a tendency toward suppuration. It causes a local dilatation of the blood-vessels, and thereby the formation of alexins and consequent greater capacity for resisting the spread of infection. Thick layers of gauze are saturated with alcohol and then covered with some impervious material. The dressing is left in place for days at a time, resaturating it with alcohol once every twelve hours. Graeser (Münch. med. Woch., July 17, 1900).

Following combination recommended as a clean and effective substitute for the ordinary lead and laudanum dressing:—

℞ *Morphinæ acetatis.*. 0.65 Gm. (1 gr.).
  Liq. *plumbi subace-*
    tatis .... 30 c.c. (1 oz.).
  Alcoholis ...q. s. ad 120 c.c. (4 oz.).
  M. Sig.: Apply on 1 layer of muslin or cotton and allow to evaporate. W. Brady (N. Y. Med. Jour., April 24, 1909).

The benefit derived from the use of the tincture of arnica in **sprains,** and spirit of camphor in **mastitis,** seems to depend entirely on the cooling produced by the rapid evaporation of the alcohol contained in these preparations. The benefit derived from the popular "alcohol rub" is entirely a matter of suggestion, and its supposed strengthening properties are mythical. Alcohol is not absorbed when rubbed on the skin. When used in this way in depressed conditions, it is liable to do harm, by reducing the body temperature when it should be sustained. Olive oil or cacao butter should be used instead of alcohol in massage. G. A. Graham (N. Y. Med. Jour., May 8, 1909).

Alcohol recommended as a final application in all cases of **wounds,** dress-

ing with either plain or carbolized gauze. In **bruises** and **sprains** equal parts of extract of witchhazel and alcohol, applied as hot as can be borne, gives much better results than liniments or any of the clay and glycerin mixtures, and is much more agreeable to the patient. In **burns** and **scalds,** with suppuration, alcohol is an ideal application, and where carbolic acid is indicated it can be used in any strength if followed immediately with alcohol. This also applies to **suppuration** in all kinds of wounds. In patients confined to bed for any length of time, the use of alcohol after bathing **prevents bedsores.** Alcohol is one of the best antiseptics to clean instruments outside of an operating room. The hypodermic needle will always be ready if kept in alcohol, and there will be no need of inserting wires in it. It is best not to use a weaker solution than 60 per cent. of alcohol. Care is required, however, to get pure alcohol, as so many inferior brands are offered, which, if used, give disappointing results. S. S. Royster (Intern. Jour. of Surg., Oct., 1909).

Reports concerning the therapeutic uses of alcohol in dermatology have recently been reviewed by Bulkley. In **eczema** Unna recommends an alcohol dressing having the following composition: Sodium stearate, 6 parts; glycerin, 2.5; alcohol, to make 100. This has the advantage of greater permanency of effect than the rapidly evaporating pure alcohol, can be employed where the application of a bandage is impracticable, is non-irritating and strongly bactericidal. In **herpes simplex** as well as **herpes zoster,** the virtues of alcohol, applied on cotton and renewed at frequent intervals, were pointed out by Leloir and Dupas; if it be applied in the stage of erythema the eruption will disappear in a few hours; if in the vesicular stage, in the course of a few days. Leloir recommends that a small quantity of

phenol be added, in order to alleviate further the burning and pain. In **lupus erythematosus,** striking results were obtained by Hebra, Jr., and by Kohn from the frequent application of alcohol,—40 to 50 times daily. Continued applications of alcohol led to cure in a case of **favus** reported by Cantoni. In **acne rosacea,** Abrahams has given subcutaneous injections of 20 to 30 drops of 95 per cent. alcohol, repeated at most three times a week, and found that, after a temporary local anemia, the injections produced a hyperemia lasting for some hours, by which obliteration of the dilated vessels could be secured, providing the treatment be kept up for two or three months.

In **frost-bite, insect-bites,** and **itching** conditions in general the local anesthetic property of alcohol comes into play. According to Lauder Brunton, the itching in **pruritus ani** can be checked with absolute alcohol.

In **sprains** and **contusions** a rubefacient as well as a cooling effect is exerted.

In **fever** the body temperature may be lowered by bathing the surface with alcohol, diluted with 2 parts of water.

Applied to **aphthæ** or **sluggish ulcers** of various kinds, alcohol, undiluted, acts as a stimulant to the processes of repair.

Used hot in a 10 to 20 per cent. solution, alcohol has long been used as a gargle in **tonsillitis** and **pharyngitis.**

In the prophylaxis of **bed-sores** and of **cracked nipples,** dilute alcohol is very effective when systematically rubbed over the areas exposed, hardening the skin so that it is rendered more resistant to external influences, and bringing an increased amount of blood to it, thus antagonizing

local necrosis. Where the nipples are already the seat of fissures or excoriations, alcohol will not only tend to relieve discomfort by obtunding the sensory nerve-endings, but will harden the surrounding healthy skin and, by coagulating the albumin in the secretions of the raw surfaces, cover these areas with a thin, protective film. The same astringent property of alcohol is of value in the treatment of **hyperidrosis** (excessive sweating) and **tender feet.**

As a hemostatic, alcohol is of some value in **minor hemorrhages,** especially where there is merely an **oozing** of blood from ruptured capillaries.

As a solvent of fatty substances, and likewise as a bactericidal agent, alcohol is of value when applied to the hands and operative area previous to minor surgical procedures. The removal of fatty material from the skin surface facilitates the action of germicides, such as mercury bichloride, subsequently applied. According to von Bruns, the value of alcohol in the **preparation of the skin before operations** is due not alone to its solvent and germicidal properties, but also to the fact that it hardens the skin and thereby keeps the deeply lodged bacteria from coming to its surface. That this factor in the action of alcohol is not in reality of great moment, however, would seem to be suggested by the recent experimental work of Ritchie, which tends to minimize the importance of the sweat-glands and hair-follicles of the normal skin as restive places for bacteria.

Advantages of **skin disinfection** with alcohol pointed out. If the skin is bathed and shaved, then rubbed for five minutes with sterile gauze saturated with absolute alcohol, its disinfection is accomplished more perfectly than by any other physical or chemical method.

Dehydrated alcohol **or wood alcohol** may be used instead of pure grain alcohol in order to save expense. For effectiveness it is essential that the alcohol used be nearly or quite absolute alcohol. Meissner (Beiträge z. klin. Chir., S. 198, 1909).

Experiments with von Herff's method of **disinfecting the hands** with acetone alcohol. It is thought that the combination of acetone enables the mixture to be used on all portions of the body, and attacks the fatty tissue and disinfects it more thoroughly than alcohol alone. The use of the nailbrush may be omitted, and a longer disinfection is obtained by this method. The use of soda solution for ten minutes increases the efficiency of the method somewhat. As the method is a simple one, it is especially adapted for the use of nurses and midwives. In the clinic the alcohol employed was 95 per cent., and the proportion of acetone, after some experiment, was fixed at 10 per cent. The most efficient combination, however, seemed to be that of 50 per cent. alcohol and 50 per cent. acetone. Preliminary cleansing with soap, water, and brush was omitted. Four minutes were occupied in disinfection. The method did not seem to irritate the skin, and one of the staff, who acquired eczema through other methods of disinfection, was much improved. Oeri (Zeit. f. Geb. u. Gyn., Bd. lxiii, Hft. 3, 1908).

Two years' experience has demonstrated to the author's satisfaction the superiority of this simple and convenient method over all other techniques in which soap and water are permitted. He rubs the field of operation for five minutes with the 10 per cent. alcohol acetone solution and then applies a varnish, the formula for which is 10 parts each of benzoin and dammar resin in 100 parts ether, stained with 20 per cent. of an **alcohol iodoiodide** solution (7 parts iodine, 5 parts potassium iodide and 100 parts alcohol). Von Herff (Therap. der Gegenwart, Dec., 1909).

Comparative tests of various methods of **sterilization** performed. A 5 per cent. alcohol solution of tannin sur-

passes all the other techniques with the exception of tincture of iodine; it ranks with this, while it is free from its disadvantages. The tannin solution is applied to the hands for two minutes and to the field of operation for one minute; the previous use of water does not affect it. Zabludowski (Deut. med. Woch., March 2, 1911).

A bacteriological and histological study of the action of alcohol on hands previously infected with bacterial cultures, showed that after 10 minutes' contact of the hands with alcohol, scrapings from the epidermis and material obtained beneath the finger nails yielded no bacterial growth on bouillon in 15 trials; on gelatin the results were negative 25 times, and positive 5 times. Other experiments showed that 10 minutes is the proper time to keep the hands in contact with alcohol for surgical disinfection; that the greater the concentration of alcohol used, the more complete the disinfection; that hands disinfected with alcohol, dried, and kept covered with a sterile compress, remain sterile for at least 15 minutes, while if kept immersed in sterile water they remain sterile for 20 minutes. Marquis (Revue de Chir., Mar., 1912).

The writer tested alcohol as a disinfectant and insecticide, and found that, when used instead of solution of formaldehyde and in quantities of 4 or 5 times larger, germs were killed as effectually. He found alcohol of 70 or 80 per cent. strength best adapted for the purpose. The germs used in the tests were cholera vibrios, typhoid and colon bacilli and staphylococci, all on silk threads. They succumbed with alcohol fumes exactly as in parallel tests with solution of formaldehyde. Arkhipiants (Russky Vratch, xvi, No. 2, 1917).

In a study of alcohol sterilization, the writer found that alcohol makes its way rapidly into the cells when the superficial tension of about 0.4 is reached. Once inside the cells, it combines with the salt present in the bacteria and induces an irreversible precipitation of the protoplasm which signifies the death of the bacterium. Higher concentrations of alcohol do not have this effect but merely suck the water out of the protoplasm, which dries up the bacteria, but they are very resistant to drying. The power of alcohols to penetrate the thin layer of grease on the skin parallels their bactericidal power, as both are the effect of the same cause, namely, a low superficial tension and high solvent power for water and lipoids. And of all the alcohols, propyl alcohol is the most efficient. J. Christiansen (Hospitalstidende, Jan. 17, 1918).

Finally, the value of alcohol as a preventive and curative agent in **carbolic acid burns** is well recognized. The phenol is dissolved by the alcohol.

Internally, there are but five indications for alcohol that justify its use under our present knowledge: (1) As an **antidote to carbolic acid**—only when it can be administered shortly—within one or one and a half hours—following the poison. Life saved in two instances by this measure. Diluted alcohol (50 per cent.) is better than brandy and whisky. (2) As a fuel, in **fevers,** exhausted states of the body, and **marasmus** of infants. Here our purpose must be to give only a quantity that the patient can metabolize or oxidize and derive therefrom energy. When we can detect alcohol on the breath, the dose must be decreased. An average dose of alcohol for this purpose is 2 to 4 c.c. (4 to 8 c.c. whisky; 30 c.c. or less of wine, according to variety; 10 to 30 c.c. of any of the "medicinal" proprietary foods), given every four to six hours, with or following other food, preferably. (3) For the **chill of febrile stages**—such as **pneumonia, malaria, septicemia**—here alcohol in medicinal dose (*e.g.,* 15 c.c. or more of whisky) opens the surface capillaries that are contracted in chill and so gives a sense of warmth to the patient, lowers the fever, and through cerebral depression blunts the pa-

tient's mental anguish. Of course, the chill of hemorrhage, shock, or other condition not accompanied with fever contraindicates alcohol. (4) To reduce **fever.** In some cases of **typhoid,** where the plunge or sponge bath fails to lower an excessive temperature, 30 c.c. of brandy immediately preceding the bath will insure a notable reduction, by driving the warm blood to the surface to be returned cooled to the internal organs. In the presence of a low arterial tension or a very weak heart muscle, however, this use of alcohol would hardly be justified. (5) As a **narcotic,** in many persons of advanced years and a few with earlier arteriosclerosis who are apt to suffer from **insomnia,** a "night-cap" of brandy in the form of a "sling" will act favorably and is free from the unpleasant symptoms that often follow the use of the old or new hypnotics. Fear of habit, in this instance, need hardly be considered. Prescribing alcohol to enable a patient to withstand the strain of having a tooth extracted, an abscess opened, or wound sutured, on the other hand, is crude therapeutics. William Brady (N. Y. Med. Jour., Apr. 24, 1909).

Alcohol Injections.—Neuralgia and Neuritis.—Injections of alcohol into or in the vicinity of nerve trunks for the purpose of relieving pain are employed particularly in **trifacial neuralgia** (tic douloureux) and in **sciatica,** but have also been utilized in intractable neuralgias of other nerves, in **neuritis** following influenza, in **blepharospasm,** and recently in **laryngeal tuberculosis.**

The Schlösser plan of injection in **tic douloureux,** viz., the injection of alcohol into the second or third divisions of the trifacial nerve at their emergence from the cranium, has been extensively tested and, owing to the prompt benefit it affords, is growing in favor, though it cannot be considered as a uniformly curative measure, a certain number of

cases relapsing after a variable number of months of freedom from pain. The mode of action of the alcohol in these cases was elucidated in 1910 by Schlösser, who found through animal experimentation that alcohol of 70 to 80 per cent. concentration, when brought in relation with a nerve, caused degenerative processes to take place in all the elements of the nerve except the neurilemma. Leszynsky, reporting 15 cases of **tic douloureux** successfully treated by alcohol injection, stated his belief that this method is practically equivalent to a section of the nerve, with the added advantage of absence of an operative scar. The method is not applicable, however, to neuralgia of the first division of the trifacial, a certain amount of danger having been found to attend injections of this branch.

> Alcohol injections given in 75 cases of unmistakable **tic douloureux,** invariably with relief. Thirty-six patients were between 60 and 70 years of age, 13 between 70 and 80 years, and 1 over 80 years. Patrick (Jour. Amer. Med. Assoc., Dec. 11, 1909).

Benzyl Alcohol Injections.—This product, available in the shops under the name of **phenmethylol,** was introduced by Macht, in 1918, as a safe and efficient local anesthetic, acting on sensory nerves and on nerve conduction. It is used in 1, 2, and 4 per cent. solutions hypodermically. It is said to be very efficient, though comparatively free of untoward after-effects.

> Clinical and experimental studies showed that benzyl alcohol is an efficient local anesthetic when administered in aqueous solution. It is soluble up to 4 per cent. in water in physiologic saline. Its low toxicity as compared with that of commonly employed alkaloids such as cocaine; the ability of the organism to metabolize it and excrete it in an innocu-

ous form; its high boiling point and the consequent ease of sterilization; the comparatively low price of the drug and the ease of its production are its salient advantages. D. I. Macht (Jour. Pharm. and Exper. Therap., Apr., 1918).

Laryngeal Tuberculosis. — Alcohol injections into the superior laryngeal nerve for the relief of dysphagia in tuberculosis of the larynx were introduced by Hoffman, of Munich. Recent experiences with this procedure have only served to confirm and establish its usefulness as a palliative measure. Fishberg has employed the procedure in many cases and obtained relief for the patient in about 50 per cent.

> Alcohol injections into superior laryngeal nerve employed in a series of cases with gratifying results. The duration of the relief experienced is the striking feature of this method of treatment. The solution employed consists of 2 grains of hydrochloride of betaeucaine in an ounce of 80 per cent. alcohol. The patient being placed horizontally, the sound side of the larynx is pressed toward the middle line with the thumb of the left hand so that the affected half projects distinctly; the other fingers of the hand lie on this half. The index finger enters the space between the thyroid cartilage and the hyoid bone from without until the patient announces that a painful spot has been reached. The nail of the index finger is now placed upon the skin in such a way that the point of entrance for the needle lies opposite its middle. The needle is pushed in for about 1.5 cm.; this distance is marked off on the needle perpendicularly to the surface of the body. According to the thinness of the subcutaneous layer of fat, the perforation has to be more or less deep. The needle is then carefully moved so as to seek a spot at which the patient feels pain in the ear. The syringe, filled with the alcohol, warmed to a temperature of

45° C. (113° F.), is screwed to the needle and the piston slowly pressed down. The patient now feels pain in the ear, the passing off of which he indicates by raising his hand. During the operation swallowing and speaking must be avoided. The injection is kept up until no further pain occurs in the ear. Then the needle is removed and collodion applied. The point of the needle is bevelled much more obtusely than the ordinary hypodermic needle, to avoid the danger of puncturing a vessel. Dundas Grant (Lancet, June 25, 1910).

Tumors. — Carcinoma of the uterus was treated with alcohol as long ago as 1879 by Hasse, who made injections into the circumference of the tumors in 3 cases with good results; after twenty-three years the patients were alive and well. Obliteration of the blood-vessels and shrinkage of the tumor were found to have taken place, through connective-tissue proliferation around the growth. A similar plan of treatment has also been utilized in **cancer of the breast.**

As a palliative measure, interstitial injections of alcohol were used by Vulliet, of Geneva, in inoperable cases of **uterine cancer.** The benefit obtained was ascribed by him to the local ischemia induced.

ALCOHOLISM, OR ALCOHOL INEBRIETY.—DEFINITION.— Alcoholism is frequently defined as the result, in the organism, of excessive consumption of alcohol. The term, thus interpreted, should refer only to individuals profoundly poisoned and diseased from this specific cause. Modern research has shown, however, that there exists a large class of cases in which the excessive use of alcohol is a predominant feature, but which are not accurately described by the term "alcoholism," viz., those in which the

use of spirits is only symptomatic of a neurosis of different nature and causation. It is probable that at least 50 per cent. of all so-called alcoholics have suffered from disease of the nervous system before acquiring the alcoholic habit.

Inebriety, meaning a poisoned or stuporous state directly or indirectly the result of alcohol, is, in reality, a more general term than "alcoholism," since it refers to the condition of all those who use alcohol to excess. This term is also employed, however, to designate toxic states resulting from the use of various other drugs, such as opium, cocaine, chloral, chloroform, etc.

TOXICITY OF THE ALCOHOLS.—All alcohols are poisonous, though their toxic power varies considerably in accordance with the variety of alcohol ingested. Thus, the heavier members of the series (propyl, butyl, and amyl alcohols), which have a higher boiling point than ordinary ethyl alcohol, are more toxic than the latter. Methyl alcohol, though the lightest of all the alcohols, is, nevertheless, more poisonous than ethyl, forming an exception to the general rule that the toxicity of the alcohols rises with the increase in their molecular weights. The toxic action of methyl alcohol, or "wood spirits," will be described later (v. Methyl Alcohol, Vol. VI). That of ethyl alcohol, which forms the subject of this article, is modified, to a certain extent, by the nature of the preparaton containing it. Spirits exert a more rapid toxic effect than wines or beers, owing to the greater concentration and quantity of alcohol present in the former. The different kinds of spirits themselves exhibit differences in toxicity in accordance with the material from which they are produced, the variations being due to differences in the amount of certain additional toxic compounds contained, such as aldehyde, ketones, furfurol, ethers, etc. Thus, according to Dujardin-Beaumetz and Audigé, spirits made from wine (brandy) are the least toxic; next follow in order spirits made from perry, cider, grain, beets, and molasses; finally come spirits made from potatoes and sorghum, which are the most toxic, owing to the relatively large proportions of isobutylic and amylic alcohols they contain. Spirits of inferior grade are especially dangerous because they are made with impure alcohol, the disagreeable taste and odor of the impurities being masked by admixture of artificial flavors and essences (Pouchet). In addition to the true spirituous liquors already referred to, there is a large group of liquors representing a solution of various aromatic principles, either of vegetable origin or produced synthetically, in a menstruum of alcohol. Here the effects of the aromatic principles are added to those of alcohol, and these fluids may, therefore, be divided into two groups, according as the tendency of the aromatic principle contained is to produce epileptiform convulsions (best illustrated in the case of absinthe), or to bring on stupor (anise, mint, angelica, etc.).

The fatal dose of alcohol varies within wide limits. The factors influencing it include not only the individual's habits with respect to alcoholic indulgence, but in addition his state of health, the climate and temperature, and the rapidity of absorption (Pouchet). The average lethal dose has been stated to be 60 to 180 Gm.

(2 to 6 ounces, approximately). Less than 1 pint of whisky has sufficed to cause the death of an adult. In the lower animals, Lussana and Albertoni give 6 Gm. (1½ drams) per kg. of body weight as the minimum lethal dose.

VARIETIES.—There are two forms of alcoholism: (1) the *acute,* in which alcoholic poisoning is speedily manifested in active excitement and disturbance, or in which a sudden exacerbation of the disorders attending the chronic type gives rise to a correspondingly marked symptomatic activity; (2) the *chronic,* in which the continued ingestion of alcoholic beverages in more or less considerable amounts sets up gradually progressing pathological changes in the various organs and tissues, thereby giving rise to chronic disorders of each of the parts thus affected.

Under acute alcoholism are to be considered not only acute alcoholic poisoning, intoxication, or "drunkenness," but also acute alcoholic epilepsy, acute alcoholic hysteria, acute alcoholic delirium or delirium tremens, and acute alcoholic mania or mania a potu.

ACUTE ALCOHOLISM.

DEFINITION.—A condition resulting from the ingestion, within a short period, of alcohol in sufficient quantity to produce exaggerated physiological effects or actual poisonous effects. The amount required to intoxicate varies widely according to the natural susceptibility of the individual, and to whether or not his organism has become accustomed to the action of alcohol through repeated use.

> After long-continued over-indulgence in alcohol (7 to 10 years) an individual develops delirium tremens.

The disease usually manifests itself in three stages—the incipient form, the fully developed classical form, and the comatose form (wet brain). The writers, who see about 2500 cases of alcoholism every year, find that about 10 to 15 per cent. of the cases of delirium tremens pass into the comatose form. The transition from delirium to cerebral edema is fairly well marked. The semi-coma which succeeds the active delirium is striking, and the delirium now becomes the low muttering type. The symptoms of wet brain are essentially meningeal—semi-coma, generalized hyperesthesia, and muscular rigidity (Kernig's sign and neck rigidity) standing out prominently; the more marked are the latter two features the graver is the prognosis. The cerebrospinal fluid is to all appearances normal. The mortality is nearly 75 per cent. Sceleth and Biefeld (Amer. Jour. Med. Sci., June, 1915).

SYMPTOMS.—Three stages are discernible in this condition: The first is that of beginning vascular relaxation and primary excitation. The intoxicated individual is usually lively, merry, agile, and joyous; all excitement and energy; in the highest spirits, cheerful, hopeful, and communicative; mercurial and confiding, often telling of his private affairs to strangers. There is a warm glow on his countenance, and he appears at his best. Gradually his spirits rise still higher; he becomes more demonstrative in love or in argument, more emphatic in his gestures, more furious in his fun, and very much louder in his laughter as the second stage is ushered in. With this he becomes much less reasonable and amenable, incoherence of thought and speech gradually sets in, the imagination revels, exaggeration is a prominent feature, and the emotions dominate the subject, intellect, reason, will, and con-

science rapidly fading into the background. In some cases his thoughts, speech, and actions are exaggerated. In other instances they are transformed, the habitually modest, retiring man becoming a boaster and a braggart, the truthful a liar, the meek violent. With all this, the speech thickens, the lower and then the upper limbs cease to act in unison; the intoxicated cannot stand, but staggers with a paralytic unsteadiness, the muscles becoming flabby and feeble. The third stage, that of "dead drunkenness," reveals the subject unconscious, with the pallor of apparent death on the face, extreme coldness of the skin, accompanied by total insensibility, and an utter disregard of the "world without." Sensation, perception, volition, and emotion, all are absent. Through this living death there lingers in the heart the only spark of vitality that keeps the unconscious drunkard alive, till the faculties have emerged—if, indeed, they do emerge—from the depth of narcotism into which they were plunged. The first, pleasurable stage, and the second stage, less pleasant, may vary in intensity and duration, but the third stage, that of insensibility, usually lasts from six to twelve hours (Norman Kerr).

In the first stage, that of exhilaration or apparent stimulation, there is an increase of the heart-rate, and frequently a rise in the blood-pressure. The breathing is generally hastened and becomes deeper. The skin is reddened, and the surface temperature rises slightly, owing to the paralyzing effect of the alcohol on the superficial blood-vessels, through which an increased amount of warm blood, therefore, courses. The pupils are of normal size or slightly dilated, and the higher psychic processes—those involving contin-

ued attention, reflection, judgment, self-control—gradually fall in abeyance.

The manifestations of the second stage are similar to those of the first, but more pronounced and with the added presence of motor inco-ordination, due to the effects of the drug on the cerebellar and spinal centers. A subjective feeling of intense peripheral warmth is experienced, the pulse is full and bounding, and the respiration hurried and frequently irregular. Incoherence of speech and staggering gait are the most prominent symptoms of this stage, though the relative time required for the appearance of each varies notably in different individuals, some getting drunk first "in the legs," others "in the tongue." Nausea and vomiting may also appear, and toward the close of the period facial pallor and a tendency to syncope may be present.

In some instances the first and second stages, instead of showing the individual in a condition of general excitement, are characterized by depression of spirits, merging more or less insensibly into the ultimate stage of total cerebral inaction. In another group of cases, on the other hand, the initial excitement is unusually pronounced, the subject crying out loudly, experiencing illusions, and even committing acts of violence.

The third stage of alcoholic intoxication, that of unconsciousness and deepening coma, is characterized by successive abolition of the functions of various portions of the central nervous system. The spinal cord and cranial nerve-centers becoming depressed, motion and sensation are progressively lost. The subject cannot be awakened by shouting in the ear; his musculature, including the sphincters, is completely relaxed, and general sensibility is abol-

ished. The pulse may be full and approximately normal in rate, or may be feeble and slow. The breathing is slow, labored, and sometimes irregular —an indication of beginning paralysis of the medullary centers. It is also stertorous, owing to relaxation of the muscles of the soft palate. The skin is now pale and covered with cold sweat, though the face is bloated, the lips purplish and swollen, and the conjunctivæ markedly congested. The temperature of the body is lowered, the rectal reading being invariably reduced by 1, 2, or even 4° F. (Butler). The pupils may be dilated, especially in cases of severe intoxication, and the light-reflex abolished. The knee-jerks and other reflexes are likewise lost.

In cases terminating fatally, death takes place from respiratory arrest after a period ranging from one-half hour to fifteen or twenty hours (Pouchet).

When an unusually large amount of alcohol has been taken—true cases of acute alcohol poisoning, as distinguished from those of ordinary "intoxication"—the stages of excitement are apt to be of very brief duration (especially if the alcohol has been taken on an empty stomach), the subject sinking promptly into coma. Vomiting, swallowing movements, piercing cries, and muscular contractures betoken a brief primary excitation of the nerve-centers, after which depression quickly appears, indicated by respiratory and circulatory disturbances and general anesthesia. Convulsions and death from respiratory paralysis or edema of the lungs may finally result.

Acute alcoholic intoxication in some instances brings forth phenomena foreign to the conventional manifestations already described. Thus, in some cases,

an *epileptic attack* is the most prominent result. It may occur either in an individual already subject to epilepsy, in which event the alcohol acts indirectly, being merely an exciting cause of the paroxysm; or, it may take place as a direct result of the effects of alcohol, in persons previously not subject to epileptic seizures, under which circumstances the condition may be termed a true *acute alcoholic epilepsy*. Again, an outburst of *acute mania* may be the result of alcoholic intoxication. Such a result is seen most frequently in cases of incipient or fully developed general paralysis. Similarly imbeciles and epileptics are particularly likely to experience hallucinations under the influence of alcohol, and to commit acts of violence upon the impulse of the moment (Pouchet). Finally, *hysterical paroxysms* may also result from the consumption of alcohol, even in relatively small amounts, and in individuals otherwise never hysterical (Kerr).

DIFFERENTIAL DIAGNOSIS. —In the first two stages of acute alcoholic intoxication, those of excitation and of motor inco-ordination, the symptoms present are sometimes distinguishable with difficulty from those produced by the ingestion of other drug excitants, such as opium, or from those of apoplexy, unless, as is frequently the case, a clue to the cause of the disturbance is furnished by the finding of alcohol on the premises, or a history of alcoholic indulgence can be obtained. In the case of apoplexy, however, the uncertainty is not likely to be of long duration, the symptoms of excitation soon passing off entirely, or being promptly replaced by coma.

A more important and difficult distinction is that to be made between the third stage of intoxication by alcohol,

Differential Diagnosis of Acute Alcoholism.

	Acute Alcoholism.	Uremic Coma.	Apoplexy.	Concussion of the Brain.	Opium Poisoning.	Diabetic Coma.
Consciousness.	Not absolutely lost; can usually be aroused by shouting or shaking.	Completely lost.	Partially or entirely lost.	Rarely completely lost.	Profound stupor.	Completely lost.
Temperature.	Often subnormal.	Variable; not uncommonly subnormal.	Usually rises above normal.	Subnormal.	Often subnormal.	Subnormal.
Pulse.	Frequent; later weak.		Slow, full, tense.	Frequent and weak.	Slow, full.	Frequent.
Respiration.	Stertorous.	Often Cheyne-Stokes.	Slow, stertorous, and puffing.	Slow and shallow.	Very slow.	Long-drawn inspiration, sighing expiration.
Pupils.	Usually dilated; equal, and react to light.	Normal or dilated.	Dilated or contracted; sometimes unequal.	Usually dilated; equal, and react to light.	Contracted.	Dilated.
Skin.	Face flushed.	Waxy pallor.	Face flushed or cyanotic; sometimes pale.	Cold and pale.	Face flushed, sometimes cyanosed.	Sometimes cyanosis.
Reflexes.	Sluggish or abolished.		Lost on paralyzed side and often on sound side.	Sluggish or lost.		Lost.
Convulsions.	Uncommon, except in dangerous cases.	Common.	Usually only at time of stroke.	Late, if any.	Uncommon.	Rare.
Paralyses.	None.	Rare.	Hemiplegia.	Transient, if any.	None.	None.
Odor.	Alcoholic odor of breath.	Urinous odor sometimes.	None.	None.	Laudanum odor on breath sometimes noticeable.	Sweet odor of breath.
Urin.	Contains alcohol; otherwise not characteristic.	Contains albumin, casts, and decreased urea.	Not characteristic.	Not characteristic.	Not characteristic.	Glycosuria, acetonuria, diaceturia.
Emunctories.	Frequently incontinence of urine and feces.	Anuria common.		Retention of urine; incontinence of feces.	No involuntary evacuations.	
Special signs.		Edema of face and feet; albuminuric retinitis.	Deviation of head and eyes to side opposite that of paralysis.	Probably evidence of trauma to head.		

that of sleep and insensibility, and comatose conditions, such as uremia, apoplexy, concussion of the brain (in cases of fractured skull), acute opium or chloral poisoning, and diabetic coma. In police stations so-called "drunks" are often not such, and a fatal result may thus be practically insured. An alcoholic odor of the breath is, of course, characteristic of alcoholic intoxication, but it is not pathognomonic; an individual unconscious from another cause may, perhaps, have taken or been given alcohol in quantity insufficient to intoxicate.

Though, according to quite a number of observers, pressure on the supra-orbital nerves in their respective notches will elicit signs of life in the alcoholic when it would not in other states of unconsciousness, the fact remains that mistakes have been, and are still, frequently made in the dif-

ferential diagnosis between ordinary cases of "drunkenness" and cases of fractured skull. It may, indeed, in some instances be practically impossible, even for the medical expert, to form a correct opinion as to the causative agent until time has been given for the disappearance of the alcoholic symptoms.

To facilitate the recognition of the morbid condition that may be present, the chart (see p. 516) is presented.

PATHOLOGY.—The most prominent of the post-mortem appearances in fatal cases of acute alcoholic poisoning is cerebral congestion. While no noteworthy destructive lesions of the cerebral substance proper may be found, hemorrhagic extravasations may quite frequently be discovered in the meninges at the base of the cerebellum, in the subarachnoid space, or even in the lateral ventricles (Pouchet).

Marked congestion of the lungs and respiratory passages is also commonly a feature. The right heart cavities may be found distended with semifluid blood. Tardieu in one case discovered apoplectic extravasations of blood in the lungs. The gastrointestinal mucous membranes may also be markedly congested, though such a condition is, of course, in no sense peculiar to alcohol poisoning. In the case cited by Kerr, of a man found dead after a drinking bout, "the mucous membrane of the stomach was so inflamed and angry, with patches of a deeper hue extending over the pyloric surface to the duodenum, and a grumous, slightly muco-purulent exudation from bleeding points, that arsenical poisoning was suspected." Hepatic congestion we would naturally expect to, and frequently do, find as a post-mortem evidence of acute alcohol poisoning.

Dana studied the brain-cells in 10 cases of acute alcoholism by the Nissl method of staining with methyl violet: (a) patients who died of alcoholism with all the symptoms of meningitis showed congestion of the membranes (pia, arachnoid), with some edema in their texture; (b) microscopic examination rarely showed any migration of leucocytes or anything approaching encephalitis; (c) the larger (pyramidal and giant) nerve-cells showed pigmentation to an intense degree, the pigment being diffused through the cell-body; (d) the cytoplasm showed various degrees of degeneration (fatty and granular); (c) the cell-body generally was shrunken, and the nucleus partially so; (f) pericellular nuclei had proliferated, and were freely present in the pericellular sacs. In cases where death was due to exhaustion the shrinkage of cells was marked.

In examining the bodies of persons dying from delirium tremens, Le Count found alterations so regularly in the cortex of the adrenals that he was led to seek the reason for the changes. The changes consist in a more or less striking diminution of the yellow color of the normal cortex. In very marked instances a reddish brown color is assumed, with only occasional irregularly distributed areas of yellow, or there may seem to be entire absence of that color. The glands were removed, the fat dissected away and then fixed in a 10 per cent. dilution of liquor formaldehydi, and after a few days the transverse segments were frozen and sectioned. As controls for this work, the adrenals from persons meeting sudden death were used and sections prepared the same way. The adrenals from 34 persons dying from delirium tremens were compared with the controls, and in practically every instance the doubly refractive droplets in the delirium tremens ad-

renals were diminished slightly, moderately, markedly, very markedly, and sometimes entirely absent in a given area. E. F. Hirsch (Jour. Amer. Med. Assoc., Dec. 19, 1914).

The introduction of alcohol into the stomach greatly increases the catalase of the blood, while the introduction of alcohol directly into the vascular system decreases the catalase of the blood. The latter morbid effect is due to the destruction of the catalase by the alcohol. Burge (Amer. Jour. of Physiol., Dec., 1917).

TREATMENT. — In common drunkenness, where the pallor and depression are not too marked, and where the respiration is active and the pulse is good, the patient may be allowed to sleep. The elimination of the poison occurring rapidly, he awakes after several hours with more or less headache, depression, irritability of the stomach, and tremor as results of the intoxication. Light and easily digested food, Vichy and milk as beverages, and a light aperient, if required, will soon be followed by recovery. Ammonium carbonate, 1 dram (4 Gm.) in a glassful of water, will counteract depression. Alcohol for the latter purpose should never be given.

In severe cases in which there is a tendency to coma, with shallow breathing and feeble pulse, the probability that a quantity of alcohol is still present in the stomach should be borne in mind. The stomach should be emptied by means of the stomach tube and washed out with warm water. External heat should be applied, especially to the abdomen and feet, and the patient placed in a warm room. Depressing emetics are contraindicated, since the depression is already excessive and the dangerous

feature. No alcohol should be administered as a stimulant. Hypodermic injections of strychnine, atropine, or digitalis are of great value to restore the equilibrium of the circulation.

In acute alcoholism attended by excitement and perhaps convulsions, especially in robust patients, free emesis should be procured promptly by giving $\frac{1}{10}$ grain (0.006 Gm.) of apomorphine hydrochloride. This usually causes vomiting in four or five minutes, and is then followed by relaxation and sleep. Digitalis or digitalin has also been recommended in this class of cases to counteract the morbid effects of the poison on the heart and circulation, and thus restore the patient to his normal condition much sooner. Hot (105° F.) rectal enemata of saline solution are also valuable in these cases during the acute attack to reduce the toxicity of the blood, if the enema is retained long enough to insure absorption. Hypodermoclysis should be resorted to if the rectal injections do not prove satisfactory.

As sedatives paraldehyde or amylene hydrate is often used with advantage. Veronal has been found especially effective by Von der Porten in 15-grain (1 Gm.) doses repeated in 3 then 5 hours until sleep is produced.

The value of apomorphine hydrochloride in acute alcoholism was pointed out by C. J. Douglas, of Boston, in 1899, but remains almost unknown. The drug acts promptly when administered as an emetic in doses of $\frac{1}{10}$ or $\frac{1}{8}$ grain, and it acts with almost equal promptness when administered as an hypnotic. The alcoholic, however wild or noisy, will, as a rule, be peacefully sleeping in ten or twelve minutes after $\frac{1}{20}$ to $\frac{1}{30}$ grain is administered subcutaneously. This sleep may last several hours,

when the patient awakens refreshed and sober. Douglas employed the remedy, with these doses, in over 200 cases, mostly alcoholics, including cases of delirium tremens, and with gratifying results. Drs. Coleman and Polk, of Bellevue Hospital, New York, used it in over 300 cases of alcoholism; also with gratifying results. Dr. Rosenwasser, inebriatist to Newark Dispensary, Newark, N. J., has also used apomorphine in the same manner, and for the same purpose, and with equally satisfactory results. The dose administered was from $\frac{1}{30}$ to $\frac{1}{20}$ grain. With these doses, the hypnotic effect is secured in 67 per cent. of the cases. Even $\frac{1}{40}$ grain, in the author's experience, is effective with some patients. A. M. Rosebrugh (Can. Jour. Med. and Surg., Oct., 1908).

Apomorphine is of great value in acute alcoholism. The desire for liquor in these cases becomes imperatively dominant. Apomorphine enforces sleep, and when the patient awakens his chain of thought has been broken and the attack is over in many cases. In all such cases the action of an emetic is of some value in sobering the patient and diminishing or abolishing the desire for more drink, and, therefore, the dose usually given is $\frac{1}{10}$ grain by hypodermic injection, adding $\frac{1}{30}$ grain **strychnine** if the heart is acting poorly. Whenever possible when given the injection the patient should be lying in bed, and basins should be in readiness, as the action of the drug is rapid. The author has always been able to secure the hypnotic effect. In many cases $\frac{1}{30}$ grain given hypodermically will be found sufficient to induce sleep. If the general condition of the patient is fair the dose may safely be repeated in about three hours, if necessary, as the drug is not cumulative in its action. C. A. Rosenwasser (Med. Times, Dec., 1910).

The injection of **magnesium sulphate** with the aid of **lumbar puncture** is also recommended.

The writer withdraws cerebrospinal fluid by **lumbar puncture,** in amounts as large as possible—50 to 60 c.c. An equal amount of sterile 1 per cent. **sodium bromide** solution is then injected with a syringe. Immediate improvement in delirium usually occurs, followed by temporary return and then permanent disappearance of delirium. Relapse occasionally after a few days is usually controlled by repetition of the injection. S. P. Kramer (Boston Med. and Surg. Jour., Oct. 30, 1913).

In using **magnesium sulphate, lumbar puncture** should be performed and 10 to 40 c.c. ($2\frac{1}{2}$ to 10 drams) of spinal fluid withdrawn. Then 1 c.c (16 minims) of a 25 per cent. solution of magnesium sulphate is injected for each 25 pounds of body weight. The withdrawal and injection should be made with the patient in the sitting posture and he should then be lowered to one of semi-recumbency. Constant attention is required for 24 hours after the injection to secure nourishment and proper care of the bladder and rectum. The treatment produces prompt relaxation. E. A. Leonard (Jour. Amer. Med. Assoc., Aug. 12, 1916).

A study of 76 cases in the St. Louis City Hospital, in 34 of which the only treatment was a **lumbar puncture,** and in the other 42 treatment was by **magnesium sulphate, paraldehyde,** and **bromides,** with **digitalis** if the pulse was rapid. The cases treated by simple lumbar puncture without medication remained in the hospital on the average 3 days, the same as the others, but they left virtually recovered, whereas those treated otherwise left in shaky, nervous condition. The average amount of fluid withdrawn was 28 c.c. with a maximum of 50 and a minimum of 10 c.c.; the average pressure was 109 (water) with a maximum of 220 and a minimum of 65. The iodoform test revealed the presence of alcohol with certainty in 30 of the 34 cases; it was questionably present in 3, and absent in 1. The Nonne-Apelt and

Noguchi tests were positive in 29 of the 34 cases. Barnes and Hein (Jour. Mo. State Med. Assoc., Nov., 1917).

The following is the routine treatment for delirium tremens: Catharsis by means of calomel followed by a rather large dose of **Epsom salts,** because of the effect of sulphate of magnesium in dehydrating the tissues of the body. Ten drops of tincture of **digitalis** and of **nux vomica** by mouth every 3 hours. In the active stage of delirium **strychnine** and **digitaline** are given hypodermically. This stimulation the writer believes to be perhaps the most essential part of the treatment. In severe cases **spinal puncture** is resorted to as soon as the patient begins to have hallucinations. The cerebrospinal fluid is always under pressure and from 30 to 60 c.c. is usually withdrawn. This procedure is followed by a rapid reduction of the delirium, especially in cases which have had preliminary stimulation and alkalinization. If the delirium returns, spinal puncture is repeated, and the fluid is usually found to be again under pressure. If the delirium still continues in spite of the spinal puncture, or if the patient is pale and covered with perspiration with a low, muttering delirium, an intravenous injection of **normal saline solution** is given, or better, **Fisher's solution.** H. H. Hoppe (Jour. Nerv. and Med. Dis., Feby., 1918).

CHRONIC ALCOHOLISM.

DEFINITION.—A condition resulting from the long-continued use of alcohol in excessive amounts. As was stated to be the case with acute alcoholism, the quantity of alcohol necessary to cause harmful results varies considerably in different persons. The manifestations of chronic alcoholism are varied. Many symptoms due to toxemia and functional derangements closely simulating or-

ganic changes are observed in the beginning. Later evidences appear of true organic disease, affecting one or more organs or systems of organs in individual cases. Thus the stomach, the nervous system, the circulatory organs, the kidneys, the liver, are all common seats of special invasion. In many cases the symptoms are very complex, and are not such as lead to the discovery of any particular organic lesion. As already stated, the alcoholism is itself sometimes secondary to a neurosis of other nature, in which event complexity of symptoms is to be expected.

Dipsomania signifies a condition, hereditary in origin, in which uncontrollable desire for alcohol is present at intervals only, the patient being free of alcoholic tendencies in the intervening periods.

Delirium tremens is another special manifestation arising from the prolonged effects of alcohol on the brain. It will be discussed later in a separate section of this article.

SYMPTOMS.—Most cases will exhibit in the beginning deranged digestion, fermentation in the stomach and bowels, constipation or diarrhea, muffled heart-sounds, irregular action with high-tension pulse, and increased dullness over the liver, perhaps with tenderness in spots. There is very commonly trembling, the hands are unsteady in their movements, the reflexes are diminished or absent, and there are areas of extreme tenderness over the body, while numbness of the limbs, rheumatic pains in both the lower and upper extremities, congested conjunctivæ and retinæ, and defects of both sight and hearing are often present. The patient may complain of anorexia, insomnia, chills, and frequently talks

about malaria as the cause of his symptoms. The urine is likely to be of high specific gravity, and to show albumin and an excess of phosphates. Chronic catarrhal conditions of the pharynx and larynx, dilatation of the skin vessels, sometimes pustular eruptions, are other early symptoms often seen.

At a later period the symptoms are more likely to point to certain structures of the body upon which the alcohol has exerted its chief effect. They may be grouped as follows:—

(1) *Digestive System.*—Chronic gastritis is a very frequent result of alcoholism. The patient complains of anorexia, nausea and vomiting, acute pain over the stomach, and constipation. The breath is foul and the tongue coated. These symptoms, usually most marked in the morning, the subject finds to be best relieved by further use of alcohol. The relief is but temporary, however, and when it ends the difficulty is increased.

> Gastritis and achylia are the rule, but a number of factors combine to induce them, not only the liquor but the irregular meals and habits of life of persons addicted to alcohol. Achylia was pronounced in 50 per cent. When they enter the hospital and get regular food and rest, the stomach usually rapidly recuperates and, as the gastritis subsides, the achylia subsides with it. Determination of the pepsin may be important for the prognosis, as the achylia did not retrogress in the few with apepsia. The discovery of inadequate pepsin secretion therefore prophesies permanent achylia. Vogelius and Wiltrup (Hospitalstidende, Mar. 15, 1916).

Long-continued alcoholic intoxication produces in some cases pronounced structural changes in the liver, most frequently cirrhosis, with contraction of the organ, or fatty infiltration, with increased size. The symptoms of the former are those of chronic catarrh of the stomach and intestines (anorexia, nausea, flatulence, constipation, sometimes light-colored stools),—which is favored by the congestion caused in these organs through compression of the portal vessels,—together with others directly due to the same condition, such as hemorrhages from the lower esophagus, nose, pharynx, or even the stomach or intestines; hemorrhoids; distention of the veins of the face, especially the nose, or of other portions of the body, usually combined with flushing due to overfilled capillaries; occasionally jaundice. Later there may appear ascites, edema of the right pleura or of the lower extremities. Enlargement of the spleen is common late in the disease. Fatty infiltration of the liver produces no such distinctive symptoms, since there is no portal obstruction. The organ shows a moderate increase in size, but its functions are not markedly altered.

> Fahr reports a series of 309 autopsies performed at the Hafenkrankenhaus (harbor hospital) of Hamburg on victims of chronic alcoholism dying from either alcoholism alone or from other causes, no less than 98 being suicides. In nearly all the cases the alcohol had been taken in the form of spirits, not as beer or wine. The results of these autopsies are distinctly not in harmony with the conception that alcohol is a poison which produces widespread and gross anatomic changes throughout the body, or that it is a common cause of either arteriosclerosis or nephritis. Even cirrhosis of the liver is far less common in alcoholics than it is usually supposed to be, for, of the 309 cases, in but 11 was cirrhosis the cause of death; in 2 other bodies there was an advanced cirrhosis, but death was due to some other cause. Of 100 cases of cirrhosis in which autopsies were per-

formed by Simmonds in Hamburg, alcoholism could be excluded in 14; in 60 it was evident, and in 26 there was no reliable information as to alcohol; therefore, it must be concluded that, while only a very small proportion of drunkards suffer from cirrhosis (about 4 per cent.), there are not a few cases of advanced cirrhosis which are not due to alcoholism, although alcohol is responsible for far more than a majority of all cases of cirrhosis. On the other hand, in nearly every case of habitual drunkenness the liver shows fatty changes, usually severe, but not ordinarily associated with connective-tissue increase, and this is by far the most frequent change in alcoholism. Editorial (Jour. Amer. Med. Assoc., Nov. 27, 1909).

The writer from his immense experience with wine drinkers in Italy is able to detect much exaggeration in many articles published. The actual amount taken daily and the proof of the wine are of great practical significance. There is a utilizable limit. The use of small amounts with meals only is regarded as innocuous. A "small bottle" of wine which contains from 20 to 30 grams of alcohol answers this requirement. Anywhere from 40 to 70 grams alcohol daily is regarded as the limit of safety beyond which a definite action on the nervous system may be perceptible. A daily consumption of from 300 to 600 grams of wine means the same thing. The writer concludes that a minimal use of wine is not only innocuous, but perhaps salutary. Bianchi (Riforma Medica, Oct. 23, 1916).

(2) *Nervous System.*—In many cases alcohol acts most prominently as a motor paralyzer, the control over the muscles being greatly impaired. The hands are unsteady in their movements, and protrusion of the tongue is imperfect. Ultimately paralysis is a possibility.

In other cases cerebral symptoms are especially marked, the prolonged action of the narcotic having caused a gradual loss of mental power. Normal cerebral activities are replaced now by exhilaration, again by depression. The subject becomes sluggish mentally, weak morally, and loses in memory and will power. He may also show great irritability, or be in a continuous state of excitement. His ideals are changed, and egotistic tendencies appear. Later, evidences of abnormal cerebration may occur in the form of varying delusions and delirium. Permanent dementia is the terminal stage in this morbid chain of events, the patient becoming in his delusions timorous, suspicious, and sometimes grandiose. The symptoms of simple or multiple neuritis are also very frequently seen in cases of alcoholism, occasionally to the extent of permanent local paralysis (see Alcoholic Neuritis under NEURITIS).

Alcoholic insanity presents special characteristic features which it is not difficult, in the majority of cases, to distinguish from other analogous conditions. Acute cerebral alcoholism presents 3 states: delirious, confusional, and stuporous. The intensity of these states varies according to whether we deal with a subacute form or with delirium tremens.

The chronic form leads inevitably to dementia. In the course of development of the latter, delusions with hallucinations and illusions may and may not manifest themselves.

In the latter symptoms it may sometimes present a picture of any other psychosis; this resemblance is only apparent, as in the majority of cases close observation will enable us to find the proper interpretations.

If the symptoms characteristic of cerebral alcoholism sometimes develop in individuals affected with other psychoses who happen to commit excesses, or do so because of the perverted mode of thinking or feeling caused by the psychoses, it does not follow that alcohol is capable of

producing these psychoses. The conception of alcoholic melancholia, mania, paranoia, or paresis is unscientific. Alfred Gordon (Jour. of Inebriety, Winter, 1908-9).

(3) *Circulatory System.* — Alcohol causes irritation of the intima of the vessels and gradual degeneration of the vascular walls. The symptoms produced are those usual in widespread arteriosclerosis: vertigo, hemorrhage or thrombosis of the cerebral vessels, etc. The heart and kidneys are very likely to be involved as a result of the same changes and undergo corresponding alterations in function.

In some instances the heart seems seriously affected. The patient complains of distress and pain over the precordial region, with alternate feelings of exhaustion and exhilaration. The pulse is frequent, and surface congestion is very intense. The heart may become dilated.

Blood-pressure estimates were made in a series of 150 soldiers, all aged 42 to 43 years. Among the 16 sober subjects, only 6.25 per cent. showed high blood-pressure; of 53 moderate drinkers, 7.54 per cent. showed high pressure; of 57 heavy drinkers, 17.54 per cent., and of 24 very heavy drinkers, 25 per cent. The conclusion is reached, therefore, that alcoholism is an important factor in the etiology of arterial hypertension. C. Lian (Bull. de l'Acad. de Méd., Nov. 9, 1915).

(4) *Kidneys.*—Chronic parenchymatous nephritis is not uncommonly caused by prolonged alcoholic excesses. Its manifestations include disorders of digestion, increased vascular tension, anemia with characteristic translucent pallor, tendency to swollen face and extremities, together with more or less distinctive changes in the urine. The latter consist of abnormalities in quantity (at first diminished, later increased), lower specific gravity, albuminuria; granular casts, sometimes fatty; epithelial and waxy casts, and decreased proportion of urea. The late symptoms include marked weakness, general anasarca, dyspnea on exertion, and uremia.

Report of observations made on a German guide in Berlin some years ago. The man regularly drank over 20 liters (quarts) of beer a day. He started with a couple before breakfast, 4 between breakfast and lunch, a couple of liters at lunch, 3 more before dinner, and the remainder between dinner and bedtime. Most of it was the strong Munich beer, with 6 to 8 per cent. of alcohol. The man thus consumed over 37 ounces of absolute alcohol a day. Yet he did not exhibit the least sign of inebriety. The case proved to the writer's satisfaction that where alcohol is diluted 20 or 30 times with water, it is almost non-intoxicating.

In view of the enormous quantities of beer consumed in Berlin, he sought in the hospitals evidences of cirrhosis or other signs of alcoholic poisoning. He found no more than would be shown by any other city of its size.

In Munich, he was told, there are some evidences of cardiac hypertrophy, due to the strain of pumping so many gallons of fluid through the kidneys. Walter (Brit. Med. Jour., Nov. 6, 1920).

DIAGNOSIS.—This is facilitated if a history of excessive use of alcohol —at times in the form of proprietary remedies—be obtainable. If not, alcoholism is suggested by the presence of symptoms such as those given in the beginning of the section on symptoms, these representing mainly functional derangements and toxic effects, but few of them being the results of organic alterations. Active treatment is then begun. Under rest, restricted diet, and hydrotherapeutic measures many of

these symptoms disappear, leaving only those expressive of permanent lesions.

A careful re-examination at the end of two or more weeks will now indicate how many of the symptoms were functional, and which of them seemingly were organic departures from health. The special effects of the alcohol on particular organs or systems of the body are ascertained by noting the presence of symptoms referable to them, such as have already been mentioned under that heading. It must be admitted, however, that in many cases the symptoms will appear very complex and refer to no particular seat of organic disease.

At this second examination the diagnosis of the patient's psychic state can also be made with some accuracy. This should comprise a study of the patient's powers of reasoning, of his ideals, of his ethical conceptions of life, of the end and object in living, of his purposes and ambitions, of the effects of losses and mental strains on his character, of the dominance of certain passions and unrestrained emotional activities, and of the presence of morbid impulses and egotism. The inquiry should extend to the everyday habits of the patient. Not infrequently periods of unexplained absence from home and business, and of unexpected and obscure conduct, will be revealed. Such occurrences justify the inference of the paroxysmal use of alcohol. Often the pronounced convictions of the patient as to the cause of his condition are significant of the use of spirits, which he denies. The diagnosis can then be made with great clearness not from what he says, but from the facts he conceals or appears to be trying to cover up.

Material assistance will sometimes be derived from a study of the family history and past medical history. Hereditary tendencies, the diseases of childhood, profoundly exhausting fevers, and injuries to the body may all be of importance in reaching a decision.

> The heredity element in inebriety is considerable and is undoubtedly a powerful predisposing cause in inebriety. A history of decided intemperance in the parents existed in over 40 per cent. of the writer's 700 cases, while 15 per cent. gave a history of defective ancestry; insanity, neuropathy, drug addiction or tuberculosis being present on the maternal or paternal side. Approximately 5 per cent. of the patients showed pre-existent mental symptoms which could be differentiated. Some of these were distinct cases of psychasthenia, others were of the milder forms of manic-depressive insanity. Neff (Boston Med. and Surg. Jour., June 16, 1910).

The influences and conditions surrounding the subject at the period of puberty, the effects on him of losses and failures early in life should likewise be ascertained, since they may have a marked bearing on the establishment of vicious habits. If alcohol has been taken, no matter how moderately at first or at what long intervals, its influence upon subsequent morbid developments should be given due consideration.

Where the symptoms are complex and the diagnosis obscure, it is usually safe to give prominence to alcohol as a causative factor. In many such cases alcohol is used to conceal the taking of other drugs. The diagnosis can then only be a tentative one, the strong probability of an alcoholic neurosis being, however, kept in mind. It may have to be altered at any time upon the discovery of new facts in the patient's history or in his present condition.

PATHOLOGY.—In this are included changes in a large number of organs and tissues. It has been shown, indeed, that alcohol has destructive effects on protoplasm in general. Hence, cellular elements of all kinds are open to its action, though it has been recognized that it is the most highly differentiated cells, such as those of the nervous system, which are the most easily affected. Its influence on the cells is exerted by reduced oxidation and altered metabolism. Destroyed cells, in virtue of a low-grade inflammatory process it produces, are replaced by connective tissue. The effect of alcohol in diminishing oxidation is most prominently expressed in the failure to oxidize fats normally, with consequent accumulation, as in the liver and subcutaneous tissues.

PROGNOSIS.—This is generally very favorable. Statistical studies in well-conducted institutions show that at least one-third of all the cases are permanently restored. The statements that 90 per cent. are cured have reference to present conditions, and are probably true for a limited time. On the turn of the drink cycle relapse occurs, and later recovery.

> The largest insurance companies in America and in England show statistically that the average mortality rate among total abstainers from alcohol is 68.4 per cent. of the expected rate, whereas that of the non-abstainer is 91.5 per cent., a difference of 23.1 per cent. This means a reduction of two and a third years in the average life of a non-abstainer. W. E. Porter (Med. Rec., Oct. 20, 1915).

Statistics of cure are unreliable. In the treatment by gold chloride 95 per cent. were claimed to be cured. At the end of one year after treatment 55 per cent. had relapsed. At the end of the second year another 20 per cent. began to drink again. In the third only 10 per cent. continued temperate and free from spirits. On the other hand, at Binghamton, N. Y., where the first exhaustive study was made of the subsequent history of 1100 patients, ten years after they had been treated, the results showed 61 per cent. still temperate and well. These and other statistics, while open to error, clearly suggest that at least $33\frac{1}{3}$ per cent. may be reasonably considered permanently restored.

The future of the inebriate depends largely on the removal of the exciting causes, whatever they may be, and their avoidance in the future. In a certain number of cases there is a complete cessation and physiological change in the organism in which the impulse to use spirits passes away forever. This is now well known. It cannot be predicted, but it occurs so often that we cannot but credit the results to greater knowledge, and to the use of more exact means in the treatment.

It may be stated that the prognosis is always good, even in cases that have apparently reached the terminal stage. This prediction refers specifically to the craze for alcohol. This dies out, is overcome by drugs and rational treatment, while other conditions of degeneration may remain.

The alcoholic or inebriate is a compound of a great variety of causes, the removal of which brings about cure. Sometimes those causes are very insignificant, sufficiently so, in fact, to be readily overlooked.

> The use of tobacco changes the prognosis greatly, according to the writer, who has arrived at these conclusions against his previous prejudices. Among those alcoholics who

have otherwise a good prognosis, the chances are even that he will return to alcoholism if he is a cigarette smoker. If he smokes a pipe or cigar the chances are about 3 to 2 that he will not return. If he does not smoke at all the chances are about 8 to 2 that he will not return. Lambert (Boston Med. and Surg. Jour., Apr. 25, 1912).

TREATMENT.—This resembles the prognosis in uncertainty and wide variations, indicating beyond question that the subject has been scarcely touched. Both hospital and home treatment, and even moral measures, show examples of permanent restoration. The field is very wide and largely unknown.

> Soon after prohibition was enforced, the deaths in Petrograd during the first 4 months decreased by 50 per cent. and for some months even more so. During the 3 months preceding the writer's paper, however, it had risen again to the former standard, or even higher, owing to the drinking of denatured alcohol, furniture polish and other substitutes for vodka. Therefore the effects of prohibition are not decisive. Novoselsky (Roussky Vratch, No. 15, 1915).

Home Treatment.—First, there is the home treatment, *i.e.*, care given to the patient in his own home by the family physician. It is evidently possible to restore many persons, particularly if they give their full assent and co-operation and carry out the measures laid down for them.

Home treatment requires implicit confidence in the medical adviser, and should consist of the absolute withdrawal of spirits and the use of means and measures to restore and relieve the conditions of starvation and poisoning present.

While the causes differ in each case, their removal and the after-treatment are substantially the same. Thus, one whose living, both in regard to nutrition and rest, is bad requires a change. Nerve rest and regular diet must be a part of the treatment.

In one who has become poisoned by spirits and highly stimulating foods, the withdrawal of these agents and rest are essential. Probably **hydropathic measures** to insure elimination by means of the skin represent the most effective method of treatment.

Many of these patients are suffering from delusional egotism and inability to recognize their condition (constantly overrating their strength), and are unwilling to use the means so evident to others. The family physician should be dogmatic and exact the use of means and measures that will break up the impulse to use spirits. He should treat the patient mentally as well as physically, and the danger of the situation should never be minimized; he should not permit the patient to think that he can depend on his own will to overcome his diseased impulses. In many instances the patient is impressed with the gravity of his disorder. He must be urged to make radical changes in his living and conduct. If his work is indoors, a change to out-of-door life is requisite. If he has neglected proper exercise, this should be arranged for in some satisfactory way.

> The writer has employed **hypnotic suggestion** in 1284 cases of alcoholism, principally chronic. Favorable results were obtained in 80 per cent. In view of the ease of application and freedom from any bad effects, the author urges the general employment of this method. Zausailoff (Roussky Vratch, Aug. 4, 1912).

Everything that will change the present current of thought with mental and physical activity belongs to rational

treatment. Of course, with this, appropriate remedies and measures to neutralize and diminish exciting causes will suggest themselves to the physician. He should recognize that these are often border-line cases in which both reason and will are clouded and the patients are irresponsible. They need suggestion, forcible and emphatic; physical treatment, and persistent use of all therapeutic means. The family physician can do a great deal in this field if he will prepare himself for it and study the peculiarities of the patient.

Office Treatment.—This is equally promising in results where the patient is recognized by the physician and his condition understood. Drug treatment forms a very important part of the means to bring relief. Probably the most practical drugs are combinations of **strychnine** and **atropine**, given at short intervals for a few weeks, then replaced by some other agent.

> Favorable report of treatment, essentially that first proposed by McBride, which consists in the hypodermic injection of **atropine** and **strychnine** twice or thrice daily for a month or six weeks, with attention to general hygienic condition, and tonics by mouth. Patients were told that success depended on regular attendance. The writer reports 7 cases, all presenting marked degrees of alcoholism. In 5, treatment was commenced in September, 1905; July, 1907; March, 1908 (2 cases), and July, 1909, respectively. These cases had remained cured up to date. W. Asten (Lancet, Nov. 6, 1909).

> Reference made to Ferran's **anti-alcoholic serum**, obtained by administering wine to horses. The serum is collected when the animal presents reactions on the part of the system corresponding to those of acute alcoholism. The serum was tried clinically in chronic alcoholics. Subcutaneous injection of the serum seemed to afford to the system improved powers of resistance against intoxication. The patients experienced a marked sense of euphoria after the injection, and were enabled to react against the exhaustion or "suppression neurasthenia" arising from complete cessation of alcoholic imbibition. Berillon (Prasse méd., Dec. 6, 1919).

The impulse to drink may be effectually controlled by small doses of **apomorphine** given hypodermically or by the mouth. Concentrated aqueous infusion of **quassia** given every hour very quickly breaks up the drink impulse, and frequently destroys the taste for tobacco, which is often a very important factor in the use of spirits.

In the office treatment care should be exercised not to substitute for spirits narcotic drugs that are likely to produce poisonous effects if taken without caution. Chloral hydrate is one of these drugs, commonly administered, but it is unsafe and dangerous; also many forms of opium and its derivatives.

Humulus is a narcotic of great power at times, and is often an excellent substitute for spirits. It is not wise to give tinctures to patients who come to the office for treatment. Give infusions always. **Salines** are very practical measures and can be given freely without risk.

Office patients of this class want remedies that will impress them at once; hence, the physician must study the drugs whose effects are more or less certain. **Sodium bromide** is a favorite drug, and can be used with safety; only, the physician must realize that it is cumulative in its action, and that **baths, cathartics,** and

diuretics are to be associated with its use constantly.

Office patients should be urged to take daily baths and **exercise in the open air,** but should be impressed psychically with the need of avoiding causes which lead or predispose to exhaustion. It is impossible to specify particular drugs and a plan of treatment applicable to every case.

The conditions vary so widely and the active and exciting causes depend on so many circumstances—surroundings, occupation, success or failure in life, diet and social influences, rest, etc.—that each case becomes a law unto itself, and requires a very close study of the conditions present.

Hospital Treatment.—This is far more successful, particularly in persons who have reached the later stages of degeneration. It is a common experience to have persons go to a hospital or sanatorium and recover from the immediate effects of spirits, and have a period of rest, change, and thorough elimination of the active exciting causes. They can then return to the family physician and remain under his care for an indefinite period. It often happens that hospital treatment and restraint is the only measure that has any promise of permanency. Such hospital treatment is effectual by combining hydrotherapeutics and sanitary appliances with hygienic measures specifically adapted to meet the wants of every person.

Drugs are very essential adjuncts and aid materially in restoring the vigor and metabolism of the body. Diet and exercise are also very important remedies. These, with nerve rest, change of thought and surroundings, are followed by restoration,

and where these measures are continued over a certain length of time the cure is permanent.

The actively working inebriates and alcoholics who are carrying loads of responsibility need hospital-homes in the country or by the seashore where absolute rest and quietness can displace their usual unhygienic activities. The diet, exercise, baths, electricity, tonic drugs, new duties, and new conceptions of their actual conditions must be forced upon them and become a part of their everyday life.

Here **psychic therapeutics** comes in as a very important means of treatment, and as a supplement to other and physical remedies. A sanatorium hospital will supply these needs, afford a clear knowledge of the patient's condition, and train him in the conduct he should observe in the future.

Stress laid on distinction between the willful and the will-less drinker. The former are men of great energy, who firmly believe they can protect themselves from all abuse of drink. The habit is thus readily acquired and is associated with an imperious daily craving. When they seek to resist it they only defer it by some hours. They then deliberately weigh the apparent gains with the sacrifices and make a choice. The problem is a very old one, and the wise man has often played a trick on his subconscious self and its burning desire rather than test his will too openly. Thus Cesar Borgia, after having become a heavy addict to wine, reduced the capacity of his glass by the cumulative addition of drops of melted wax until he had weaned himself from the desire. A more rapid process consists in rendering the drink nauseating by the addition of **ipecac.** The psychology of the willful drinker is best explained by the creation of a

second personality through the addiction, which is subject to its own laws. While the strong subject may become an aboulic as a result of prolonged addiction, there are others who are aboulic by nature, and who put up no struggle at all. These subjects are best adapted to **psychotherapeutic management.** Jaguaribe (Bull. méd., Mar. 17, 1920).

There are many hospitals and sanatoria with varied measures of treatment, but in none of those worthy of confidence are there any specifics enveloped with mystery. The treatment has passed beyond the empiric stage, and is now as thoroughly fixed with its positive results as that of any other disease, and there are no specifics or combinations of drugs that can effectually check the drink impulse unless at the peril of its breaking out again with greater force.

GENERAL TREATMENT.—Every inebriate is toxemic, and every attack of drunkenness is a period of exacerbation of this toxemia. The first measure is to **withdraw the spirits** and remove the poison by stimulating the bowels and the skin to insure its elimination. **Calomel,** either in a large dose of 10 grains or a small dose of 1 grain every two hours, until 6 or 8 grains are taken, together with salines, are the most effective cathartics, and should always be used at the beginning.

If the patient objects to the sudden removal of alcohol, and his condition borders on delirium, $\frac{1}{10}$ of a grain of **apomorphine** hypodermically should be given as a relaxant. This will be followed by vomiting, free perspiration, and sleep. On awakening a **hot bath** of the temperature of 105° or 110° should be given. If the patient will consent to lie in the bathtub for an

hour or two at a time, then be rubbed down and recline in a cool room, excellent effects will be obtained. If he will not, an ordinary hot bath should be followed by a vigorous hand rubbing and reclining in bed. If the desire for spirits continues and the depression is not marked, $\frac{1}{30}$ grain of **strychnine** with $\frac{1}{200}$ of **atropine** should be given every two hours.

To get a man on his feet with a clear brain, and with the craving for narcotics removed, a mixture of drugs given to the writer by Mr. Charles B. Towns has proven of value. It consists of a mixture of 15 per cent. **tincture of belladonna,** 2 parts, and 1 part each of **fluidextract of xanthoxylum** and **fluidextract of hyoscyamus.**

From 6 to 8 drops of this are given every hour, day and night, until either the patient shows symptoms of **belladonna** excess or, with the cathartics about to be described, the patient has a certain characteristic stool. This dose of the mixture is increased by 2 drops every six hours, until 14 to 16 drops are being taken; it is not increased above 16 drops. Usually an alcoholic can be given 4 compound cathartic pills (U. S. P.) at the same time that the specific is begun. After the mixture has been given for fourteen hours, a further dose of C. C. pills is given, either 2 or 4, depending upon the amount of action obtained through the use of the previous dose. If these have acted very abundantly, only 2 are now necessary. At the twentieth hour of the mixture 2 to 4 more C. C. pills are given, and after these have acted, should the patient begin to show abundant green movements, an ounce of castor oil should be given, and a few hours later the characteristic thick, green, mucous, putty-like stool will appear. Usually the mixture has to be continued, and at the thirty-second hour 2 to 4 C. C. pills are again given, and a few hours later the castor oil. The mixture can then be discontinued.

Of course, in treating alcoholics

one finds in the majority of cases the necessity to stimulate them and to give them some hypnotic, but this can be done without interfering with the hourly administration of the above. Alexander Lambert (N. Y. State Jour. of Med., Jan., 1910).

The belladonna treatment properly given will totally eradicate the physiological craving for narcotic drugs, including alcohol. To secure permanent results it is necessary to pay as much attention to the after-care in both alcoholic and drug cases as is given to the derivative treatment. This after-care consists in regular supervision over several months and a thorough understanding of the needs of the patient by both himself and his friends. The treatment consists in the hourly administration of a mixture of **belladonna, hyoscyamus,** and **xanthoxylum,** in connection with increasing vigorous catharsis at stated intervals. At the end of this course a so-called "typical stool" is obtained, and the patient emerges into a very unusually comfortable condition with little or no craving remaining. There are several points to be noted about this vigorous derivative treatment. The belladonna mixture must be pushed to the physiological limit and not beyond. Atropine poisoning must be sighted, but not reached. To fall short of this point spells failure to actually obliterate the craving; to overstep it intimidates the patient. Ross Moore (So. Calif. Pract., July, 1911).

If the restlessness and excitement continue, repeat the **apomorphine** in $\frac{1}{20}$-grain doses every two hours. Should the stomach be irritable, use **hot and cold fomentations** over it, and give carbonated waters, usually **Vichy.** The patient should not take any food, for, as a rule, digestion is impaired to the extent that food cannot be assimilated.

If the patient is restless and insists on moving about, have an attendant go with him and walk him until he shows **fatigue,** then bring him back and give a hot tub bath or shower with **apomorphine** and **strychnine.**

Never give chloral or morphine. The latter may be used under special circumstances, but the former is contraindicated. For the insomnia **lupulin, valerian, cannabis indica,** and other vegetable narcotics may be given, but never in the form of tinctures.

Often some of these drugs produce sleep at once. Others have little or no effect and should not be given. The size of the dose will depend upon the apparent sensitiveness of the patient to the effects.

Occasionally, where there is a tendency to delirium, **bromide of sodium** in from 50- to 100- grain doses may be used. Not more than 3 or 4 doses at intervals of three hours should be given. After giving this drug the patient should take a hot bath, which has the effect of producing more rapid absorption of the salt. Sometimes a **salt bath** is preferable to plain water, if there is much depression.

In the severe types of acute alcoholic delirium that have come under observation, 64 cases have all given evidence of a severe acid intoxication. The symptoms represent the effects of the alcohol on the nervous system and liver, and the pathologic changes may range from simple edema to severe degenerative changes of the fatty type. Any treatment, to be of service, therefore is indicated in the stage of edema. After experimental work with various salts that have the power of dehydrating edematous tissues, he devised a mixture of **sodium bromide, sodium chloride** and **sodium bicarbonate** that could be used in large quantities intravenously without producing the

toxic effect of bromide as ordinarily given in large doses. As the severe types also suffered from starvation acidosis, **glucose** in high concentration was also used intravenously; this not only furnished an available carbohydrate that was readily utilized by the body, but in 30 per cent. concentration produced marked dehydrating effects on the central nervous system.

In the preparation of the solutions 5.8 Gm. (1³⁄₁₀ drams) of chemically pure sodium chloride and 8.4 Gm. (2¹⁄₁₀ drams) of chemically pure sodium bicarbonate were boiled in 120 c.c. (4 ounces) of distilled water and filtered through paper, then placed in a flask and reboiled. In addition 10.2 Gm. (2½ drams) of chemically pure sodium bromide were boiled in 30 c.c. (1 ounce) distilled water, filtered and reboiled. These may be kept ready for use, and when needed are added to 850 c.c. (28⅓ ounces) of either freshly distilled water or tap water that has been filtered and boiled. Under no circumstances should old distilled water be used, as it has been found that it produced severe chills. This mixture is heated to about 110° F. (43.3° C.) and is ready for use. Both of these solutions must be given very slowly, from 20 to 30 minutes being taken for the 1250 c.c. (2½ pints) or 1000 c.c. (2 pints) employed. A small percolator, such as is used in giving salvarsan, with rubber tubing and needle attached, is all the apparatus that is needed.

The mortality was lower, 9.3 per cent.; the time of detention less, an average of 2.63 days, and the period of delirium much shortened. The patients ate better. The desire for alcohol was abolished, at least for the time being. J. J. Hogan (Jour. Amer. Med. Assoc., Dec. 16, 1916).

Cinchona bark in infusion has a very good effect, and infusion of **quassia** chips is another remedy of great value, but for the acute stages hot water, hot baths are most prac-

tical. In the course of a day or so a disgust for spirits begins. In the mean time **salines** should be given and the bowels kept loose.

The **strychnine** combination should be kept up, and should the **atropine** symptoms appear the size of the dose diminished. Food should be taken very sparingly for the first two days. After that a diet rich in **cereals** and **malted milk** may be given.

As a rule, milk is not a good diet for these cases. **Coffee** and **tea** may be used according to the taste of the patient. **Exercise** in the open air and reclining in a cool room, with nerve rest, are very essential.

The disposition of the patient to eat inordinately should be suppressed. If there is a tendency to constipation, mineral waters that are laxative on an empty stomach should be given.

According to Hall **caffeine** is almost a specific in alcoholic toxemia. This drug in doses of 1 to 2 grains every one, two, or three hours will usually, in from twenty-four to forty-eight hours, quench the thirst or craving for alcohol to such an extent that the most confirmed habitués will voluntarily abandon its use.

Elimination through the skin, bowels, and kidneys should be the main purpose of the treatment, all with proper nutrition and rest. Where there is a history of specific disease, **mercury** or **arsenic** in small doses is required. When the paroxysm subsides and the patient is restored, the great question becomes to determine the exciting causes which produce the return of the drink craze, and ascertain their periodicity.

In most cases it is wise to discontinue the strychnine compound and continue the free use of baths, care-

fully regulated diet, with salines, for some time, until evidence of the return of the drink craze appears.

If the patient keeps in close touch with the family physician his digestion, nervous symptoms, and habits of living can be studied and properly treated. Where possible, **Turkish baths,** with **prolonged rest** afterward, should be given at least once or twice a week.

If the physician can secure the full confidence of the friends as well as the patient, and impress upon him the necessity of extraordinary care and the methodical use of hydropathic measures, a great deal can be accomplished.

In the country, baths may be improvised in a tub, and water falling on the patient in a narrow stream has an excellent sedative effect. **Hot packs** or sheets wrung out in hot or cold water covering the body, over which are spread dry blankets, producing intense or rapid perspiration, are often most valuable.

The physician should always study the digestion of the patient and determine the states of acidity or alkalinity of the stomach and correct them as required.

Exhaustion and depression frequently precede a drink impulse. Small doses of **ipecac,** ¼ of a grain given at intervals of two hours, produce a pronounced relaxing effect, and where the patient has high-tensioned arteries and excitable pulse this is an excellent remedy.

Quassia chips in a concentrated solution are almost a specific for the drink craze, but they must be given in large doses at intervals of an hour or so, and followed by free use of cathartics and baths. **Quinine** has some value, particularly where there is a history of malaria, but it should not be used more than about two weeks.

All such cases are self-limited and will recover with the use of hygienic measures. The great value of the physician is to determine and remove the causes and, where there is a periodicity in the return of the paroxysm, to have the patient under treatment and anticipate this condition.

The treatment of drug and alcohol habitués with **hyoscine** will remove the desire for these drugs, thus eliminating the element which prevents the patients from abstaining by force of will power. Having lost the desire, they do very well without intoxicants or the drugs, as shown by the increase in appetite, gain in flesh, and their general improvement. The question of relapse lies entirely in the sincerity and environment of the patient. The favorable alcoholic addicts are those who earnestly desire to discontinue the use of intoxicants and are willing to change their mode of living and environment, but who cannot until relieved of the craving for liquor. Relapse in both drug and liquor cases is not due to a desire nor suffering after the treatment, but to their curiosity to test the necessity of total abstinence, or to the temptations of social life. A single dose of the drug or drink of liquor, even after 1 year of total abstinence, is very apt to start the craving, resulting in a condition which is no better than before treatment. This method may prove a valuable treatment in apparently hopeless cases of opium poisoning. Interesting experiments along this line might be carried out. The one contraindication for this treatment is the presence of Bright's disease. No patient should be treated unless put to bed and watched by competent nurses day and night during the first week. Riewel (Monthly Cyclo. and Med. Bull., Oct., 1909).

[The craving for stimulants is mainly due to the depression of the endocrins fol-

lowing their abnormal excitation by alcohol overdosage. The stage of excitement which typifies excessive metabolism and high vascular tension is replaced by virtual failure of the circulation of which the sympathetic (chromaffin) system, which includes the adrenals, sustains oxygenation, metabolism and also vascular tone particularly insofar as the arterioles are concerned. Hence the danger of too suddenly withdrawing alcohol in such patients. **Strychnine**, $\frac{1}{40}$ grain (0.0016 Gm.), to stimulate the adrenals, **posterior pituitary**, $\frac{1}{10}$ grain (0.0065 Gm.), to raise the vascular tension, and **suprarenal gland** 2 grains (0.13 Gm.), in one capsule *t. i. d.*, are efficient unless excitement prevail. In the latter case **hydrobromide of hyoscine**, $\frac{1}{200}$ grain (0.0003 Gm.), hypodermically, which owing to its stimulating action on involuntary muscles tends to constrict the dilated arterioles, followed by **potassium bromide** 30 grains (2 Gm.), to inhibit the irritability of nerve centers, should first be administered. C. E. DE M. S.]

In delirium, opium and its derivatives and many of the other drugs that are powerful narcotics should be avoided. All proprietary drugs are dangerous, and should be condemned no matter what the experience may be. Every physician is capable of doing far more for the relief of this condition by adapting the remedies to the particular case than by any widely exploited compound.

A law, dealing with the repression of public drunkenness and the supervision of saloons, has been promulgated. It imposes on persons found in a manifest state of drunkenness on the streets a fine of from 1 to 5 francs for the first offense. The second offense is punishable by from 1 to 3 days' imprisonment, and a third offense, when occurring within the first 12 months, is punishable by imprisonment for from 6 days to 1 month or a fine of from 16 to 300 francs. Any person who is convicted twice may be deprived of his electoral and civic rights for 2 years.

The law fixes an analogous penalty for such dealers as shall serve liquors to minors (under 18), and dealers who are fined more than once will be liable to closure of their establishments for a year or more. The sale of alcoholic liquors on credit is interdicted. The law forbids the employment of females under 18 years of age in retail liquor establishments, unless they are members of the proprietor's family. Dealers who encourage debauchery shall be imprisoned for from six days to six months, and shall forfeit their political rights for five years. Their establishments shall be closed permanently. Paris Letter (Jour. Amer. Med. Assoc., Nov. 17, 1917).

ACUTE ALCOHOLIC DELIRIUM, OR DELIRIUM TREMENS.

—This is a condition of acute alcoholic poisoning, associated with exhaustion and cell starvation. It occurs chiefly in habitual drinkers, but it is also observed in ordinary temperate persons after a prolonged drinking spell. Though mostly met with in spirit drinkers, it is occasionally seen in beer, wine, and cider drinkers.

SYMPTOMS.—Two forms are distinguished: the *traumatic* and the *idiopathic*. They differ little except in the prodromata. In the traumatic form, after an accident (sometimes only slight trauma) the characteristic tremors, etc., appear, frequently without warning. In the idiopathic form, the patient who is about to have an attack is restless, uneasy, irritable; he sleeps badly, if at all, suffers from digestive troubles, and has little desire for food. Delirium then appears. The patient cannot rest, but must be in constant motion. He is shaking all over ("the shakes"), is consumed with terrors, continually in deadly fright of things which he mentalls sees, or of persons whom he thinks are after him for the

commission of some crime. At other times his dread is of something terrible, though he cannot tell what it is. He is all the while trying to escape from these well-defined or undefined horrors, and, in the attempt to escape, fatalities sometimes occur.

Hallucinations of various kinds, especially of sight are most common: snakes, rats, mice, loathsome things, flames, and, in a case of the writer's, roaring lions bounding down the chimney, below the chairs, and rushing in at the windows. According to Liepmann, visions of animals are present in 40 per cent. of cases at most. The delirium is best described as one of busy wakefulness and suspicion. There is a third non-febrile, innocent form, in which the temperature does not rise above 100° F.

Hallucinations of hearing are not so common, but exist in probably 10 to 20 per cent. of cases. Delusions (false perceptions concerning self) are found in from 5 to 9 per cent.,— mostly delusions of persecution. Sometimes there is one hallucination, illusion, or delusion throughout; sometimes there is a succession.

The tongue is white and furred. Tremor of this organ, and especially of other muscles, is a more or less marked and generally present symptom.

The fever is not very high, being about 100° to 103° F. If higher, it is an unfavorable omen. The pulse is soft, rapid, and readily compressed. The skin is clammy. Insomnia is constantly present, but usually sleep and improvement occur on the third or fourth day. In unfavorable cases the patient grows gradually worse and finally dies of heart-failure (Norman Kerr).

DIAGNOSIS.—Alcoholic delirium may be mistaken for the delirium of meningitis, of typhus and typhoid fevers, and of chronic alcoholism. The history and progress of the case determine the first two, and the absence or significance of thirst, tongue trembling, and tremors the third.

> Report of tests on 8 patients showing that 325 Gm. of absolute alcohol must be ingested before any appears in the cerebrospinal fluid.
>
> It appears first in the urine, and disappears early here.
>
> In 5 other cases, alcohol found in the cerebrospinal fluid gave the clue to the diagnosis. In 3 it had been responsible for the fatal cerebral hemorrhage, at least 325 c.c. of alcohol having been ingested. In a fourth it caused irregular epileptiform seizures and impulsive violence which had been ascribed to the underlying epilepsy. In the fifth case, mental impairment and tendency to ataxia in the man of 54 were explained by the alcohol found in the lumbar puncture fluid during 18 days. When it finally disappeared from the fluid, all the symptoms subsided.
>
> The potassium bichromate and sulphuric acid test of Gréhant and Nicloux for alcohol was used. Lenoble and Daniel (Bull. de la Soc. Méd. des Hôp., Oct. 10, 1919).

Pulmonary disorders; congestion, especially when of traumatic origin, and pneumonia may also give rise to delirium simulating that of delirium tremens. Fractured ribs may thus become the primary factor of violent accesses. The same may be said of erysipelas.

PATHOLOGY.—Acute alcoholism is due to gradually produced changes in the nerve-tissues, and especially to retained products of metabolism. The cerebral lesions in alcoholic delirium are of two varieties. The first is observed in all alcoholics, and is due to the alcohol itself: atheromatous de-

generation of the vessels, the degree of disorder increasing as the caliber of the vessel is reduced. The nerve-cells also show granular pigmentation and fatty degeneration.

The second variety is derived specially from the character of the delirium, and not from the alcohol itself. It consists in congestion, hematic pigmentation in the capillaries and nerve-elements, and degeneration of the nerves and fibers of the cortex, the precursors of general paralysis (Norman Kerr).

According to Jacobson, delirium tremens occurs when a brain, deteriorated by chronic alcoholism, is influenced by a toxic agent, either due to the action of bacteria or to autointoxication from diseases of the digestive tract, the kidneys, or the liver.

The changes in the central nervous system and spinal ganglia are quite uniform; they consist essentially, first, in thickening of the walls of the arteries, proliferation of the connective tissue in the media, and dilatation and infiltration of the lymph-spaces. These changes are more pronounced in the cortex, and frequently lead to minute hemorrhages, as many as 200 of these having been counted in a square centimeter of the cortex. The capillaries appeared to be proliferated, particularly in 1 case, but they and the veins showed no pronounced anatomical alteration. The neuroglia fibers of the cortex showed, according to Weigert's new method, considerable proliferation. The Weigert cells were more numerous than normal. The free nuclei, both the small and large varieties, were increased in number in the second and sixth layer of the cortex, and appeared to be accumulated around the degenerating cells. The spinal cord was apparently normal (Tromner).

Of 247 recovered personal cases of delirium tremens studied by Jacobson, 202 were uncomplicated and 45 complicated by other diseases. Although the delirium tremens cannot be regarded as caused by the action of the pneumococcus, it resembles, in all its features, an infectious disease: it has a stage of incubation—a duration of about four days; it ends with a critical sleep; is accompanied by rise of temperature, and almost in all cases by albuminuria, and when autopsy is made the spleen is generally found to be the seat of parenchymatous degeneration, as well as the heart, the kidneys, and the liver.

PROGNOSIS.—In private practice the prognosis is favorable in ordinary cases; in hospital practice it is much less so. Of 1241 cases admitted to the Philadelphia Hospital during a fixed period, 121 died. Recurrence occurs if drinking is continued. Norman Kerr noted recurrence from one to five times in 104 out of 442 cases treated in a special institution.

TREATMENT.—The first indication is to **remove** the **causative toxemia**; this can be done by persistent and active **hydropathic measures.** Hypnotics are not always necessary, and may be dangerous. They should be avoided if possible. The best treatment is continuous baths, showers, salines, restraint, exercise, massage, good air, and little or no food until the delirium subsides. The following represents, however, the measures generally recommended in such cases:—

The patient must be kept in bed and carefully watched. Strapping in bed should not be practised, as the restraint causes muscular movements and delirium. A sheet tied across the bed is preferable, as this allows more freedom of motion. Attendants or a

padded room is best of all. **No alcohol** should be given, the strength being sustained by foods, milk, soups, etc.

> The **immediate suppression** of alcohol in delirium tremens and the employment of **hydrotherapeutic measures** advised rather than of hypnotics; the former serve to increase and to maintain the activity of the heart, although one would expect an opposite effect. In instances of cardiac weakness stimulants, **strophanthus, digitalis, camphor, caffeine,** are employed, and in about three days, when the delirium begins to lessen, 30 to 60 grains of **chloralformamide** are given; this quickly induces sleep. Thirst is controlled by bitter infusions. If pneumonia appears as a complication, digitalis and alcohol are administered. In these patients the prognosis is distinctly bad. Eichelberg (Münch. med. Woch., Bd. xx, S. 978, 1907).

Potassium bromide, ½ dram, with tincture of capsicum given every three hours, is recommended for mild cases by Osler.

Sleep is, however, deemed necessary by some authorities. According to Lancereaux, for example, the real chance of recovery in alcoholic delirium lies in **sleep.** The patient is, therefore, isolated in a quiet, dark, and, if necessary, padded room, no physical restraint being employed. To procure sleep the patient is given 1 to 1½ drams of **chloral hydrate,** with ½ grain of hydrochlorate of **morphine,** in an infusion of limes. If sleep does not come on in about ten minutes, from ⅙ to ¼ grain of **morphine** is injected hypodermically.

After the various alcoholic disturbances have subsided **strychnine** or **nux vomica** is given, followed by **hydrotherapeutic measures.** If there should be gastric complication, an antacid, such as **sodium bicarbonate,** is administered.

> The writer reports the result of five years' use of **veronal** in delirium tremens. His method of administration is as follows: An initial dose of 1 Gm. is given in all incipient cases. If sleep does not follow within three hours, another gram is given. Sleep then follows and lasts six to eight hours, or even twelve. On waking the patient is clear, quiet, and feels well. If there is yet some tremor, 0.5 Gm. of veronal is given, and by evening all tremor has, as a rule, disappeared. If the patient remains in the hospital some time longer for other reasons, 0.5 Gm. is given every evening to insure against sleeplessness. If the delirium is not controlled from the 2 Gm. as given above, another gram may be given five to six hours after the second dose. Only 3 patients have failed to respond to this treatment out of a total of 100. There were 2 deaths from double pneumonia. In all the author's experience he has only seen 1 case of veronal rash, and absolutely no other symptoms of veronal poisoning. V. F. Möller (Berl. klin. Woch., Dec. 27, 1909).

Broadbent, of London, has found very efficacious the following treatment of delirium tremens. The patient is stripped naked and lies on a blanket over a waterproof sheet. A copious supply of ice-cold water is provided, and a large bath sponge dripping with the iced water is dashed violently on the face, neck, chest, and body as rapidly as possible. He is then rubbed dry with a rough towel, and the process is repeated a second and a third time. The patient is now turned over, and the wet sponge is dashed on the back of the head and down the whole length of the spine two or three times, vigorous friction with a bath towel being employed between the **cold-water applications.** By the time the patient is dried and made comfortable, he will be fast asleep.

> Delirium tremens, on alcoholic basis, even in strong men of middle age, is a serious illness, with a mor-

tality variously stated as 3 to 19 per cent. The writer treated 396 cases from 1901 to 1906 with **chloral hydrate** (1 to 3 grains) and with **bromides.** Digitalis was given only when necessary, and alcohol was withheld. The mortality was 9 per cent. Of the cases, 17.4 per cent. belonged to the type of delirium imminens. Between 1907 and 1909, 264 cases were treated almost exclusively with **veronal.** The drug was dissolved in warm tea. Soon after admission the patient received 1 Gm. (15 grains), and one to two hours later a second gram. If necessary, a third gram is administered within five hours and a fourth gram within twelve hours. There never was the slightest untoward effect on pulse or respiration. The mortality sank to 3.4 per cent.; the percentage of cases where the delirium could be prevented rose to 28. The majority of fatal cases already suffered from pneumonia. This observation proves that veronal is far superior to chloral and bromides to check the attack in its incipiency, and also to prevent a fatal issue. Ernst v. d. Porten (Therap. d. Gegenwart, June, 1910; Merck's Archives, Nov., 1910).

Incipient cases, with insomnia, restlessness, tremor, occasionally hallucinations, should receive large doses of **hypnotics,** preferably **veronal; whisky** should be given regularly, and **ergot** at frequent intervals, either by intramuscular injection or by mouth. Discontinue medication *gradually,* and only after all restlessness and tremor has disappeared. More advanced cases, with marked delirium, incoordination, usually fever, slight leucocytosis, and profuse perspiration, should receive **veronal** in moderate doses; also **ergot.** Ranson and Scott (Amer. Jour. Med. Sci., May, 1911).

It must not be forgotten, however, that large doses of narcotics, with the cardiac depression apt to follow their exhibition, are dangerous, especially in the aged and infirm inebriates. Kerr preferred repeated doses of

liquor ammoniæ acetatis (B. P.). Sleep, thus quietly and safely induced, has proved much more curative than narcotics in his practice.

Trional and **opium,** if given, should be administered cautiously.

If fever is present, the **cold douche, bath,** or preferably the **wet pack** may be tried. If the pulse becomes too rapid and weak, very small doses of **digitalis** in **aromatic spirit of ammonia** should be given. **Digitalis** in large doses is dangerous (Osler, Delpeuch, Kerr).

The author witnessed the collapse and death of a robust man in delirium tremens while being given a prolonged warm bath. One of his patients succumbed in collapse during a wet pack, and he has consequently abandoned these measures. In treatment of 1051 cases of delirium tremens in the last sixteen years, he has made it a rule to allow no alcohol. In the first series of 486 cases the mortality was 6.37 per cent., while in the last 565 cases it has been only 0.88 per cent. He ascribes this improvement in the results to his observation of the fact that the cause of death in delirium tremens is generally paralysis of the heart, and he now addresses treatment to the heart regardless of whether cardiac symptoms are apparent or not. The agitation and motor excitement react on the heart, and signs of heart weakness soon become manifest. He makes it a rule to give **digitalis** from the very first, giving 1.5 Gm. in an infusion in the course of the day and repeating this dose two or three times. If it cannot be given by the mouth, he gives it in a rectal injection. At the first signs of heart weakness other heart tonics are used; 1 Gm. of **camphorated oil** is injected subcutaneously every hour or so until the critical symptoms subside. A tablespoonful of ice-cold **champagne** every half-hour was also found useful—the only way in which he allows alcohol. To promote the washing out of the toxins causing

the attack, he has the patients drink copiously, and supplies them for the purpose with a drink which has the color of beer and tastes refreshing, and is taken eagerly by the delirious patient. It is merely a 1 per cent. solution of sodium acetate in water to which a little common syrup has been added. S. Ganser (Münch. med. Woch., Bd. liv, Nu. 3, 1907).

The writer ascribes the symptoms of this condition to the accumulation of toxic products, autogenous as well as alcoholic, in the blood. Accordingly, he aims at the removal of these deleterious substances. He gives normal salt solution in large quantities by the rectum, hypodermically, or, if necessary, intravenously. Thus the entire circulatory system is flushed with fluid to its utmost capacity, and this is then relieved by free purgation with large and repeated doses of Epsom salt. Calomel in full doses is also given. Sparteine is administered in 2-grain doses for the purpose of supporting the heart and promoting diuresis. For the delirium itself gelsemine is given every hour, or every two hours, until its physiological effect is produced; the dose advised is $\frac{1}{25}$ grain. Alcohol is reduced to moderate limits, but is not entirely withdrawn: opium and other narcotics are condemned as not merely dangerous, but useless. Physical restraint is also held to be not permissible. In 450 consecutive cases the results of this line of treatment are described as excellent, and no death from delirium tremens occurred in the whole series. G. E. Pettey (The Hospital, Jan. 15, 1910).

The writer found that cases of acute alcoholic delirium of the severer types were suffering from acid intoxication. His treatment, therefore, was directed towards efforts to neutralize it and to favor its rapid elimination. He employed a mixture of sodium bromide, sodium chloride, and sodium bicarbonate that could be used in large quantities intravenously without producing the toxic effect of bromide as ordinarily given in large

doses. As the severe types also suffer from starvation acidosis, glucose in high concentration was also used intravenously. The solution may be given once a day or every 2 hours, according to the results obtained. In the cases given the blood-pressure was lowered after the injections. Any existing edema, as of the brain, was reduced; all the tissues of the body and the blood were dehydrated by the action of the salts. Hogan (Jour. Amer. Med. Assoc., Dec. 16, 1916).

The routine treatment for delirium tremens employed by the writer in the Cincinnati General Hospital is as follows: Catharsis is used as a routine measure, calomel, followed by a rather large dose of Epsom salts. Tincture of digitalis and tincture of nux vomica, 10 drops of each, are given by mouth every 3 hours. In the active state of delirium strychnine and digitalin are given hypodermically. This stimulation is the most essential part of the treatment. In mild cases the indication for alkalies is met by the use of the imperial drink with lemon juice. Prolonged hot baths and hot packs are given twice a day, chloral and bromids are given only at night, and then not more than 2 to 3 doses during the 12 hours. In ordinary mild cases of delirium tremens, uncomplicated with kidney trouble, the above treatment is sufficient and the disease runs a very mild course. In the more severe cases, and at present a routine treatment, spinal puncture is resorted to as soon as the patient begins to have hallucinations. From 30 to 60 c.c. (1 to 2 ounces) are usually withdrawn. The withdrawal of fluid is followed by a rapid reduction of the delirium especially in cases which have had preliminary stimulation and alkalinization. Hoppe (Jour. Nerv. and Mental Dis., Feb., 1918).

The patient should be carefully fed, milk and concentrated broths being especially useful. If necessary, nutrient enemata are to be administered.

Excellent is hypodermoclysis or the intravenous infusion of **saline solution** in delirium tremens, which increase the amount of the circulating medium in which the toxic materials are dissolved, thereby diluting the poison and bathing the nerve-centers with a more attenuated solution of the same. The amount of circulating fluid is increased above the normal, so that the excretion of fluids through all the eliminatory channels is augmented, thereby carrying off in solution much of the contained toxins. The action of the heart is improved by the filling of the relaxed vessels. These suffice to restore the physiological equilibrium and turn the balance in favor of recovery (Warbasse, Quénu).

> Comparison of the number of cases of delirium tremens and of trauma in drunken men during a period of municipal total prohibition with the period before it, and during a period of partial prohibition in that a supposedly prohibitive price had been placed on liquors. The cases of delirium tremens which had averaged 5 or 6 a week, ceased totally during the total prohibition, but the number of "drunks" was even higher than usual, the restrictive measures evidently failing in their purpose. It takes brandy to produce delirium tremens, and this is scarcely obtainable. H. I. Schou (Ugeskrift for Laeger, May 24, 1917).

ACUTE ALCOHOLIC MANIA (MANIA A POTU).

SYMPTOMS.—The patient, in a wild, ungovernable fury, shouts, stamps, strikes, or kicks, and is, for the moment, uncontrollable. The eyes roll, the face is flushed, and the veins distended and engorged; the muscles are at their highest point of tension, and are in continuous, violent action. The pulse is strong, bounding, and tumultu-

ous. Though mechanically conscious, the subject is filled with "blind fury." He is carried away in a tempest of nervous excitation and passion. The paroxysms of violence sometimes last only a few minutes, at other times for from an hour to several days, with quiet intermissions. Rarely are there delusions, though the infuriated subject may vent his violence on the first animate or inanimate object in his way. In a few cases the fury is directed against a certain person or thing. Violence is succeeded by calm; a few minutes after a storm the temperature is normal, and during the paroxysm rarely raised. In some constitutions a paroxysm may be provoked by a small quantity of alcohol (Kerr).

DIFFERENTIAL DIAGNOSIS.—It may be differentiated from delirium tremens by the absence of tremors, terror, hallucinations, delusions, the white tongue, nausea, and the delirium of the latter. Further, mania a potu may arise from a small quantity of an intoxicant taken in a short time, while delirium tremens is due to large quantities taken in rapid succession, or from smaller quantities long continued (Kerr).

ETIOLOGY AND PATHOLOGY.—Mania a potu is occasionally seen in chronic inebriates, and most frequently in periodic tipplers. In the latter it often occurs when, after an interval of abstinence, an intoxicant is freely partaken of. Some chronic inebriates invariably suffer acute mania if they drink a single glass of spirits, wine, or beer beyond their usual allowance.

The paroxysms of acute mania resemble those of epilepsy, and a large proportion of police-court drunken offenders are patients of this class. The

symptoms are evoked by the pathological action of acute alcoholic intoxication on nervous systems liable to such excitation, either congenitally or from the effects of intemperance, traumatism, or brain-tire. According to Jones, the forms of insanity met with which result from alcoholism are: 1, amnesic; 2, delusional and, 3, chronic varieties which end in dementia.

PROGNOSIS. — The prognosis is much more favorable than in ordinary acute mania, the paroxysm usually rapidly passing away, leaving the patient exhausted and peaceful. Unless alcohol be taken again relapse is rare.

TREATMENT.—But little treatment is generally needed in this condition. Non-alcoholic liquids, such as **milk**, iced milk, milk and soda, or **saline draughts** with **ipecacuanha** and **bromides** are sufficient to bring about recovery. Sometimes **cold affusions** and, in prolonged paroxysms, **wet packs** prove valuable adjuncts.

When violent mania is present, **apomorphine**, $\frac{1}{8}$ to $\frac{1}{6}$ grain, hypodermically, causes nausea and rapid sedation.

If it persists, **potassium bromide**, in 30-grain doses every two hours, or **morphine**, $\frac{1}{4}$ grain at long intervals, must be resorted to.

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ALEPPO BOIL. See ORIENTAL SORE.

ALOES (*Aloe*).—The inspissated juice of the leaves of *Aloe vera* or *A. chinensis* (Curaçao or Barbadoes aloes) or of other species, such as *Aloe Perryi* (socotrine aloes, East Africa) and *Aloe spicata* or *A. ferox* (Cape aloes). The plants are indigenous in Africa and India, and are naturalized in the West Indies and along the Mediterranean shores.

PROPERTIES AND CONSTITUENTS.—Curaçao aloes occurs in orange-brown, opaque, and resin-like masses which give off an odor of saffron and have a very bitter and somewhat nauseous taste. Socotrine aloes varies in color from yellowish brown to dark brown; its odor and taste are similar to those of Barbadoes aloes. Cape aloes is reddish brown or olive-black.

According to A. R. L. Dohme, Curaçao aloes is as efficient as socotrine aloes and less expensive; the greater portion of the latter now sold is made up of the former.

Purified aloes (*aloe purificata*), the form generally employed in medicine, is aloes which has been softened by heating and the addition of alcohol, strained, and dried. It occurs in commerce in pieces or in powder form.

Aloes contains: 1. Aloin, a bitter, crystalline principle present in amounts ranging from 4 to 30 per cent., and composed in socotrine aloes exclusively of barbaloin, to which, in Curaçao aloes, is added the isomeric body isobarbaloin. 2. Emodin (Kraemer), an actively cathartic principle. 3. A yellowish, odoriferous volatile oil. 4. A resinous material, varying according to the species of aloes. 5. Albuminous bodies. 6. Fatty substances. 7. A small amount of gallic acid.

Aloin, official as *Aloinum*, occurs as minute orange-colored crystals or as a microcrystalline powder varying in color from lemon-yellow to yellowish brown. It has little or no odor, is bitter to the taste, and remains unchanged in the air. It is soluble in 65 parts of

water and in 10.75 parts of alcohol. Its solutions turn brown on continued exposure, and when alkalies are added present a dark-red color with greenish fluorescence.

DOSE AND PREPARATIONS.

—the dose of purified aloes in adults is ½ to 10 grains (0.03 to 0.6 Gm.), the average dose being officially given as 4 grains (0.25 Gm.). The dose of aloin is ½ to 2 grains (0.03 to 0.12 Gm.). Average dose: 1 grain (0.065 Gm.). The other official or semi-official preparations of aloes are:—

Pilula Aloes, containing aloes and soap, of each, 2 grains (0.13 Gm.). Dose: 1 to 4 pills.

Tinctura Aloes (10 per cent.), containing also 20 per cent. of licorice. Dose: ¼ to 1 fluidram (1 to 4 c.c.). Average dose: 30 minims (2 c.c.).

Extractum Aloes, N. F.—A watery extract, dried and powdered. Dose: ½ to 6 grains (0.03 to 0.4 Gm.). Average dose: 2 grains (0.125 Gm.).

Pilula Aloes et Ferri, N. F., containing purified aloes, dried ferrous sulphate, confection of rose, and aromatic powder, of each, 1 grain (0.07 Gm.). Dose: 1 to 4 pills.

Pilula Aloes et Mastiches, N. F., (Lady Webster's Dinner Pill), containing purified aloes, 2 grains (0.13 Gm.); mastic, ⅔ grain (0.04 Gm.), and powdered red rose, ½ grain (0.03 Gm.). Dose: 1 to 4 pills.

Pilula Aloes et Myrrhæ, N. F., containing purified aloes, 2 grains (0.13 Gm.); myrrh, 1 grain (0.07 Gm.), and aromatic powder, ⅔ grain (0.04 Gm.). Dose: 1 to 4 pills.

Tinctura Aloes et Myrrhæ, N. F., containing aloes, myrrh, and licorice, of each, 10 per cent. Average dose: 30 minims (2 c.c.).

Aloes is also a constituent of :—

Tinctura Benzoini Composita, containing benzoin, 10 parts; aloes, 2; storax, 8; tolu, 4. Dose: 30 minims (2 c.c.).

Extractum Colocynthidis Compositum, containing extract of colocynth, 16 parts; purified aloes, 50; resin of scammony and powdered soap, of each, 14; cardamom, 6. Dose: 7½ grains (0.5 Gm.).

Pilula cathartica composita.

℞ *Ext. colocynthidis*
    comp. .... gr. i⅓ (0.08 Gm.).
  Hydrarg. chloridi
    mitis .... gr. j (0.06 Gm.).
  Resinæ jalapæ .. gr. ⅓ (0.02 Gm.).
  Cambogiæ pulveris .... gr. ¼ (0.015 Gm.).
Dose: 2 pills.

Pilula rhei composita.

℞ *Rhei pulveris* ... gr. ij (0.13 Gm.).
  Aloes .... gr. iss (0.10 Gm.).
  Myrrhæ .... gr. j (0.06 Gm.).
  Olei menthæ pip.. gr. ¹⁄₁₂ (0.005 Gm.).
Dose: 2 pills.

Pilula cathartica vegetabilis, N. F.

℞ *Ext. colocynthidis*
    comp. .... gr. j (0.06 Gm.).
  Ext. hyoscyami . gr. ss (0.03 Gm.).
  Resinæ jalapæ .. gr. ⅓ (0.02 Gm.).
  Ext. leptandræ,
  Resinæ podophylli ......āā gr. ¼ (0.015 Gm.).
  Olei menthæ piperitæ .... gr. ⅛ (0.008 Gm.).
Dose: 2 pills.

Pilula laxativa composita, N. F.

℞ *Aloini* .... gr. ⅕ (0.013 Gm.).
  Strychninæ ...... gr. ¹⁄₁₂₈ (0.0005 Gm.).
  Ext. belladonnæ
    fol. .... gr. ⅛ (0.008 Gm.).
  Ipecacuanhæ pulv. gr. ¹⁄₁₆ (0.004 Gm.).
  Glycyrrhizæ pulv. gr. ¾ (0.046 Gm.).
Dose: 2 pills.

MODES OF ADMINISTRATION.

—Aloes is entirely soluble in 5 parts of alcohol, but only partly soluble in water. It is generally administered in pill form on account of its strongly bitter taste. It acts slowly, and can, therefore, be administered at bedtime with the expectation that its effects will be exerted the next morning. Aloes may be used alone, but is oftener given in conjunction with other

cathartic remedies and correctives, as in several of the preparations above mentioned. Certain agents have been found to increase its effects, including bile, iron, and the alkalies. Equal parts of purified aloes and dried oxgall may be administered in a salol-coated pill with advantage. Aloin, while somewhat less certain in its action than aloes, is often considered preferable because of the smaller dose required and less liability to cause "griping." It is frequently employed in the aloin, belladonna, and strychnine pills, of which the official form (*Pilula Laxativa Comp.*) has already been referred to.

INCOMPATIBLES.—Aloes is incompatible with mineral acids, iodine, silver nitrate, tannic acid, phenol, menthol, thymol, and salicylic acid.

CONTRAINDICATIONS.—It is generally inadvisable to prescribe aloes in cases of hemorrhoids, owing to its effect of causing congestion of the pelvic organs; in cases accompanied by free secretion of mucous in the bowel, however, it may, on the contrary, prove beneficial. Aloes is likewise contraindicated in pregnancy and in menorrhagia occurring in plethoric women. In view of its elimination, in part, through the milk, it is not available for use as a purgative in nursing women.

PHYSIOLOGICAL ACTION.—In small doses aloes and aloin exert a *stomachic* effect. The secretions of the alimentary tract are augmented. With larger doses (2 to 4 grains) its well-known *laxative* effect is obtained, ten to fifteen hours usually elapsing from the moment of extubation until the first evacuation results. The effect is due to stimulation of the muscular coat as well as the glands of the large intestine, and is generally attended with a certain amount of griping pain. Through

its property of inducing hyperemia in the ovaries and uterus, aloes also has distinct value as an *emmenagogue.*

Though easily absorbed through abrasions and ulcerated areas (exercising thereafter its characteristic laxative and other effects), aloes exerts no local therapeutic action. It is eliminated with the feces, slightly with the urine, and, in nursing women, with the mammary secretion.

Aloin, the so-called active principle of aloes, is believed not to exert its effect in the bowel until it has undergone certain changes in composition. The resulting active compound, which can be made from the pure, crystalline aloin by boiling a solution of the latter (Cushny), is probably contained in the crude drug after the crystalline aloin has been extracted. Hence, the fact that in practice crude aloes is found to act with greater certainty and speed than the principle aloin. It has been found that in human beings placed upon an exclusive meat diet aloin acts much more strongly than in persons subsisting on a mixed diet. The aloin is believed to be altered through processes of hydrolysis and oxidation into *emodin* (oxymethylanthraquinone), an active constituent of many other drugs of this class, such as senna, cascara sagrada, and rhubarb, which induces the purgative effect. Injected under the skin or into a vein, aloin for the most part passes into the bowel, there exerting an irritant effect and inducing purgation. In the rabbit, however, in which aloin is excreted to a large extent through the kidneys, pronounced irritation of these organs is produced, catharsis being, on the other hand, an infrequent result. A nephritis is generally induced, in which the epithelium of the tubules is particularly involved,

the glomeruli being largely spared. The urine contains casts, blood, proteids, and leucocytes; it may be either augmented or decreased in quantity (Mürset).

UNTOWARD EFFECTS.—The use of aloes over long periods is said to favor the production of hemorrhoids. Large doses of aloes induce burning at the anus; sometimes blood-stained stools, painful micturition, and uterine discomfort. Dosage exceeding 0.20 Gm. (3 grains) per diem, when persisted in for any length of time, leads inevitably to intestinal irritation and congestion (Pouchet). Massive single doses of aloes may induce general prostration with slowing of the pulse and a fall in the temperature.

THERAPEUTIC USES.—**As a Laxative.**—Aloes is most frequently used in the treatment of **constipation** due to intestinal atony. In moderate doses it stimulates the intestinal mucosa to increased secretory activity, thereby facilitating the discharge of the bowel contents. Its continued use is, however, to be avoided, since on prolonged administration a tendency to aggravation of the disorder present is likely to appear.

A characteristic feature of the action of aloes is the congestion it tends to produce in the intestinal tract (especially the rectum) and pelvic organs. This property has led to its occasional use as a derivative in conditions associated with cerebral or pulmonary congestion, blood being thereby removed from the engorged area. Experimental work has shown that aloes, in common with other purgatives of the anthracene series, does not act as a true cholagogue, *i.e.*, does not increase the amount and concentration of the biliary secre-

tion. It does, however, by accelerating peristalsis, promote the removal of bile from the intestinal tract, and prevent its reabsorption from the duodenum into the liver. For the relief of **hepatic congestion,** Rendu has recommended the use of aloes in combination with calomel and gamboge. The cathartic effect of aloes has been found to be greatly favored by the presence of bile, which is believed to assist by exerting a solvent action on the drug, thereby hastening its effect. In view of this observation, too, it is thought that in cases of obstructive jaundice the action of aloes is interfered with owing to the deficiency of bile.

Alkalies and iron assist the purgative action of aloes. The former facilitate the decomposition of aloin, whereby a more strongly irritant and cathartic substance is formed. Iron similarly favors the oxidation of aloin. In **chlorosis** the aloes and iron combination is often employed, as in the official pill of aloes and iron. It is best, however, not to use this pill, owing to the particularly marked constipating effect of the preparation of iron it contains. The pyrophosphate of iron or dialyzed iron is to be preferred. Nux vomica and belladonna, or their active alkaloids, are also frequently combined with aloes, the former to improve the tone of the intestinal muscles, and the latter to prevent "griping." The last-named effect can also be minimized by giving the drug after meals.

Robin recommends the following pill as a mild, but efficient laxative:—

℞ *Aloes,*
 Ext. of liquorice ..āā **1 gr.** (0.06 Gm.).
 Gamboge .... **½ gr.** (0.03 Gm.).
 Ext. of belladonna,
 Ext. of hyoscyamus, āā **1 gr.** (0.06 Gm.).

Enough for 1 pill. Take one or two on retiring.

Aloin possesses over crude aloes the advantages of smaller bulk and less tendency to cause intestinal irritation, but these are partly offset by the diminished certainty and celerity of its action.

In large doses aloes acts as a drastic, inducing first eructations and a feeling of weight in the stomach, then copious stools with colicky pains. Its use as such, however, is to be avoided, because of the marked intestinal irritation and congestion it causes.

As a Stomachic.—In doses not exceeding 1 to 1½ grains (0.06 to 0.10 Gm.) daily, aloes improves the appetite and excites the gastric functions.

As an Emmenagogue.—In anemic women with **amenorrhea** aloes is sometimes given to favor the menstrual flow. It is best given four days before the expected period, and its action is greatly enhanced by combination with iron. In amenorrhea due to other causes the official pill of aloes and myrrh may be tried, the congestive influence of the active drug tending to facilitate menstruation; good results, however, follow less often than in the anemic cases.

In Hemorrhoids.—Though the use of aloes as a laxative is contraindicated in the presence of hemorrhoids, this drug, given in small doses, has been claimed by some to be beneficial in cases where the circulation in the inferior hemorrhoidal veins is particularly sluggish and the pile masses protrude, inducing tenesmus. The use of aloes in very small doses when hemorrhoids are associated with irritation and frequent small, thin evacuations has been advocated by Fordyce Barker.

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ALOPECIA.—Baldness; calvities.

DEFINITION. — Alopecia is a physiological or pathological deficiency or loss of hair, either partial or complete. The forms of alopecia may be classified as shown on opposite page.

Congenital Alopecia.—This commonly manifests itself either as a scanty growth, a development only in certain localities, or as a retarded appearance of the hair. In rare cases there may be complete absence of the hair due to arrested development of the follicles. In such cases hereditary predisposition is usually present, and there are apt to be, in addition, delayed or defective dentition, and at times developmental defects of the nails.

[J. H. Hill (Brit. Med. Jour., vol. i, 1881, page 177) has described a race of hairless Australian aborigines. JAY F. SCHAMBERG.]

Case of hereditary alopecia due to hypothyroidia, occurring in 3 generations, affecting equally the male and female members of the family, and limited strictly to the scalp. The affected individuals were born with a normal growth of hair which continued to grow normally until about the fourth or sixth year. It then began to fall out and lose its pigment, becoming completely colorless, and continued to do so until at puberty or a little later the scalp was completely bald. In 3 children of the family under observation the administration of **thyreoidin,** in doses of ½ to 1½ grains (0.03 to 0.09 Gm.) daily, was followed by good results. Petersen (Dermat. Zeitsch., Apr., 1915).

A diminution or absence of the secretion of the thyroid gland is known to cause the following changes in the skin: Myxedema, roughness and dryness of the skin; yellow complexion with a rather circumscribed redness of the cheeks, called the "malar flush"; dry seborrheic coating of the scalp, constituting at times a thick crust; dryness, lack of luster

FORMS OF ALOPECIA.

I. Congenital alopecia.
II. Senile alopecia.

III. Premature alopecia.

(a) Idiopathic. { Hereditary predisposition.

(b) Symptomatic. {

(1) Local diseases.

Seborrhea.
Eczema seborrhoicum.
Psoriasis.
Erysipelas.
Lupus erythematosus.
Syphilodermata.
Folliculitis.
Tinea tonsurans.
Tinea favosa, etc.

(2) General diseases.

Acute {
Typhoid fever.
Variola.
Scarlatina.
Pregnancy.

Chronic {
Syphilis.
Leprosy.
Myxedema.
Neurasthenia.
Chronic intoxications.
Anemia.
Diabetes.
Cancer.
Uric acid diathesis.
Phthisis, etc.

and wiriness and defluvium of the hair. He cites a personal case in which progressive alopecia yielded rapidly under a careful **diet** and 5 grains (0.3 Gm.) of **thyroid gland** a day. Montgomery (Jour. Cutan. Dis., Apr., 1915).

Its really important and striking features, based on a careful study of serial sections from different parts of the skin of a case were the following: there were comparatively few vessels; there was 1 arrector pili muscle; 1 abortive follicle; no hair shaft; no sebaceous glands; and no sweat glands. Blaisdell, Cunningham and White (Boston Med. and Surg. Jour., Feb. 8, 1917).

Senile Alopecia.—As the name indicates, this form of baldness is observed in the aged. With the atrophic skin changes that accompany senility there takes place a gradual thinning of the

hair, beginning upon the vertex of the scalp, the frontal and the temporal regions, and slowly leading to a more or less complete baldness of the calvarium. Under the microscope the cutis proper and the hypoderm exhibit thinning and atrophy.

Case of periodical shedding of the hair in a woman aged 21 years. Her hair was shed every winter and grew in again in the summer. Last winter she became entirely bald, and this summer her hair did not grow in again. Absence of hair existed on the general surface, which began in circular patches when she was 12 years old. H. Ledermann (Jour. of Cut. Dis., Jan., 1904).

Premature Alopecia.—This form of alopecia is encountered chiefly in individuals between the ages of 20 and 35. G. T. Elliott found that among 344

private cases of premature alopecia, 64 per cent. occurred under the age of 30. Premature alopecia may be either *idiopathic* or *symptomatic*.

In the *idiopathic* variety the scalp presents no abnormal condition. At first only a few hairs fall out from time to time, being replaced by a shorter or finer growth. Later these fall and are followed by still finer hairs. In this manner the greater part of the hair of the scalp may be gradually lost. The affection occurs in both sexes, although much less frequently and less completely in women than in men. Heredity appears to be a strong predisposing factor.

There is a growing opinion that the so-called idiopathic baldness is exceptional, and that most cases of premature alopecia are associated with seborrhea in some form. Of 344 private cases of premature alopecia studied by Elliott, 316 had seborrhea. Jackson found 75 per cent. of 300 cases due to seborrhea.

The *symptomatic* form results from various local and general diseases. Rapid falling of the hair (defluvium capillorum) commonly follows acute diseases, such as typhoid fever, smallpox, etc. Full regeneration of the hair follows the restoration to health. Rapid and extensive loss of hair occurs with frequency in the early stages of syphilis. The hair is also thinned or lost in such cachectic conditions as phthisis, myxedema, diabetes mellitus, leprosy, etc.

> Referring to the fall of the hair after influenza, the writer points out that the temples and occiput are the areas usually chiefly affected. He attributes it to the toxemia, and thinks probably it is indirectly due to the toxemia affecting the trophic nerves to certain areas of the scalp. He does not recommend cutting the hair un-

less that is necessary to carry out any special form of treatment. A. Pasini (Giorn. Ital. d. Mal. Ven. e delle Pelle, fasc. i, 53, 1919).

Alopecia Seborrhœica. — Considerable difference of opinion exists as to what constitutes the seborrheic process; the comprehension of the relation of seborrhea to baldness is thereby embarrassed. Nearly all writers are agreed that *dandruff* has not the same significance for all observers. Sabouraud holds that dry pityriasis of the scalp is not a depilating affection itself, but that it is frequently associated with the true seborrhea. Many clinicians speak of an *alopecia pityrodes* in which there is either a seborrhea with fatty crusts or a pityriasis with abundant scaling. Crocker does not restrict alopecia seborrhœica to the oily form: according to his experience there is either "an excessive greasiness of the surface from oily seborrhea, or fine, glistening, powdery scales, or greasy scales lying closely on the scalp and requiring to be scraped off, or yellowish, fatty matter looking like pale-yellow wax."

> New clinical form of atrophic alopecia, for which the term "pseudopelade" is adopted. It is a process of atrophy and sclerosis affecting the hair-covered regions of the body, especially the scalp, terminating in patches of baldness, smooth, of pseudocicatricial aspect. It seems to be closely allied to erythematous lupus and keratosis pilaris. Brocq, Lenglet, and Ayrignac (Annales de dermat., vol. i, No. 3, 1905).
>
> Analysis of 679 cases of loss of hair, chiefly alopecia simplex and alopecia furfuracea. There were, however, 86 cases of alopecia and lesser numbers due to ringworm and syphilis, and 2 cases from X-rays. Women seemed to be more affected by loss of hair, in the relative proportion of 54 to 46, but possibly they consult physicians more freely on this account than do men.

The author finds that heredity, dandruff, systemic depression, fever, operations and maltreatment of the scalp have been connected in the patients' minds with the fall of hair and, according to his figures, hereditary taint exists in 30 per cent. while dandruff was present in 443 patients, a percentage of more than 79. Systemic depression was recorded in 120 cases, fever in 63, and maltreatment was evident in 277 cases, or nearly half of the whole number. Most patients were unable to remember the date of beginning alopecia, but it seems, from all the accurate data that could be obtained, that in the clinically uncomplicated loss of hair, it began before 30 in 84 per cent. of the males. In females it appeared at this early age in a much less percentage and seemed to be of later development. Dandruff appeared also earlier in men than in women, being about twice as frequent between the ages of 16 and 25. C. J. White (Jour. Amer. Med. Assoc., Sept. 24, 1910).

ETIOLOGY AND PATHOLOGY.

—Dandruff is generally regarded as the most potent cause of baldness. It is a plausible and attractive theory to attribute the process to microbic invasion. Sabouraud has brought forth strong evidence to show that his microbacillus is intimately associated with, if not the cause of, oily seborrhea. He likewise regards this organism as the cause of baldness. The microbacillus, according to him, enters the mouth of the hair follicle, multiplies, and forms a thin microbic lamina, which separates the hair shaft from the follicular wall. Epithelial irritation causes the encysting of the bacilli in a plug or cocoon. Then follows increased sebaceous flow, hypertrophy of the sebaceous gland, and progressive atrophy of the hair papillæ. Sabouraud recognizes other causes which render the soil favorable, such as city life, insufficient

exercise, excessive meat diet, gout, heredity, etc. If baldness has a microbic origin, Sabouraud is certainly correct in regarding the above causes— causes which are operative in the busy life of great cities—as of vast importance. Premature baldness is rare or absent among savages and is less common in country than in city districts.

Many other factors have been invoked as causes of baldness, such as

Alopecia from a cured tinea favosa. (*Schamberg.*)

the too frequent wetting of the hair, the wearing of stiff hats which constrict the temporal arteries, etc. It is also stated that brain workers are particularly subject to premature alopecia; this is probably more the result of sedentary life than of intellectual activity.

Alopecia areata is often caused by traumatisms of the head. The existence of anatomical and functional lesions of the central nervous system must be admitted, the state of central irritation ·giving rise to peripheral

trophic disturbances, which manifest themselves by the appearance of hyperalgesic zones. Possibly, vascular lesions analogous with arteriosclerosis are the cause of the falling out of the hair. At any rate, the nervous lesion is the predominant etiological factor. Psychic traumatism, especially fright, has an identical effect. Weichselmann (Deut. med. Woch., Nov. 12, 1908).

Alopecia of dental origin often follows a painful attack of trigeminal neuralgia caused by the teeth (18 out of 25 cases). This attack may precede the depilation by two or three months, but more commonly it occurs in the preceding month. It occurs on the same side as the trigeminal attack, more frequently on the left side because dental lesions are more common on the left side. It appears by preference in certain predisposed zones, as if there was a relation between the seat of the dental irritation and the seat of the initial area of alopecia. Thus, in 16 cases of trouble with the lower wisdom tooth the author found alopecia localized on the same side of the nucha in 14. It follows alveolar and gingival irritation rather than dental irritation proper. Thus, in 25 cases of dental alopecia the author traced the cause in 3 cases to inflammation of the dental pulp, in the remaining 22 to troubles outside the teeth. These irritations seem to act differently upon the trigeminus. It is accompanied by certain phenomena, such as hyperesthesia, erythrosis, hyperthermia, adenopathy, lymphangeitis, and edema, grouped by Jacquet under the name of the dental syndrome. The areas are generally small in size and few in number. The prognosis is good. The cure is rapid and often immediate after dental intervention alone. Rousseau-Decelle (Presse méd., Feb. 6, 1909).

Many cases of hereditary syphilis show no sign beyond defects of dentition—defects which, in spite of the now 25-years old teaching of Fournier, are not yet, he says, sufficiently well known. The writer thinks it hardly conceivable that the teeth in these cases can have suffered without some imprint of the disease upon the viscera, nervous system, or bony structures. Such imprint does occur, and it renders the offspring of syphilitic parents more predisposed to attacks from other diseases, such as eczema, psoriasis, and alopecia areata, as regards the skin, and to tuberculosis, enteritis, and probably other internal diseases. Sabouraud (Presse Méd., Mar. 22; May 17, 1917).

PROGNOSIS. — Alopecia seborrhœica gradually progresses, unless checked by treatment, to a denudation of the vertex leaving a fringe of hair in the temporal and occipital regions. Appropriate treatment, particularly if instituted early, will sometimes check the hair loss and lead perhaps to some regrowth. If systemic conditions are present which render the scalp a favorable nidus, the outlook is more unfavorable.

TREATMENT. — The treatment must be directed toward the existing seborrheic process. The measures employed relate both to general and local treatment. **Outdoor life, exposure of the scalp to sunlight, the restricted use of meats** (Sabouraud says baldness is less common in vegetarians), the avoidance of excesses of all kinds, are to be recommended.

Such tonics as **iron, strychnine, phosphorus, arsenic, and codliver oil** may be given with advantage.

Local treatment is of great importance, particularly when dandruff is present. It consists of the proper cleansing of the scalp and the stimulation of the sebaceous glands to healthy action.

The **tincture of green soap** makes an admirable shampoo for the removal of epithelial and sebaceous *débris*. This may be advantageously followed by such a hair-wash as :—

℞ *Resorcinolis* .... ℨij (8 Gm.).
 Acidi acetici ... f℥j-f℥ij (4-8 c.c.).
 Ol. ricini ...... f℥ss-f℥j (2-4 c.c.).
 Alcoholis, q. s. ad f℥vj (180 c.c.).
 Ol. bergamott... ♏xl (2.4 c.c.).

When greater stimulation is desired, the following lotion may be used:—

℞ *Hydrarg. chlor.*
 corros. ...... gr. viij (0.5 Gm.).
 Betanaphtholis . gr. xxv (1.6 Gm.).
 Glycerini ...... f℥j (4 c.c.).
 Alcoholis ...... f℥iv (120 c.c.).
 Aquæ cologni-
 ensis .... f℥ss (15 c.c.).
 Aquæ .... f℥iiss (75 c.c.).

Sig.: Hair-wash; part the hair and apply with a small sponge.

Another lotion frequently prescribed where stimulation is desired is as follows:—

℞ *Tinct. canthar-*
 idis .... f℥vj (24 c.c.).
 Tinct. capsici,
 Olei ricini ....āā ♏xxx-f℥j (2-4 c.c.).
 Spts. myrciæ (bay
 rum), q. s. ad f℥vj (180 c.c.).

It is a good plan in many cases to use an ointment in conjunction with hair lotions. The lotion may be used each day, and the pomade applied once or twice a week. The latter should be rubbed in in very small quantities, so as to avoid disagreeable greasing of the hair. When ointments are used conjointly with washes, the glycerin or oil in the lotion may sometimes be advantageously omitted. Sulphur is the most useful agent for scalp pomades when any seborrhea is present. The following ointment gives most satisfactory results:—

℞ *Sulph. præcip.* .... ℨj (4 Gm.).
 Adipis .... ℨj (31 Gm.).
 Ol. bergamott .... ♏xl (2.4 c.c.).

Daily digital **massage** of the scalp is distinctly useful, as is also the **vigorous use of the hairbrush** to produce hyperemia of the scalp.

> Successful treatment depends upon the promptness with which one first notices that the hair is beginning to fall. Healthy hairs do not come out,

and if hairs are found on the pillow, on the clothing, or in the hairbrush, the indication is given for beginning the treatment. One of the most important yet very generally neglected, prophylactic measures consists in **frequent ablution of the head,** a measure that is still considered injurious by many people. On the contrary, frequent shampooing and rubbing of the head is the best preventive of baldness. Another feature on which the author lays much stress is the necessity for cleanliness in all utensils used in the barber shop or in private.

Actual baldness cannot be cured, but a great deal can be done to prevent its onset by properly treating the tendency to falling of the hair. A course of treatment is outlined, of which the following are the most important features: **Daily shampooing** with soap and hot water, followed by drying and the application of a 1: 1000 solution of **bichloride of mercury.** This is allowed to evaporate, and the scalp is then rubbed with a 1: 400 solution of **thymol or naphthol in alcohol.** Finally, an ointment is applied containing 1 part of **salicylic acid,** 2 of **tincture of benzoin,** and 50 of vaselin. In obstinate cases the treatment is begun by the application of **tar liniment,** which is removed ten minutes later with the soap. Lassar (Deut. med. Woch., July 5, 1906).

The most satisfactory lubricant is **cocoanut oil.** It keeps the hair soft and silky and does not mat the hair or plaster it down. A good **shampoo** about once a month suffices. The **wire brush** keeps the scalp pretty free from dirt and dandruff. By its gentle and not disagreeable friction of the scalp, it promotes the circulation and thus brings nourishment to the hair-bulbs, and gives vigor to the growing hair. S. Hendrickson (Jour. Amer. Med. Assoc., Sept. 2, 1911).

The writer considers local treatment of paramount importance, and the first part is the same for all forms of seborrhea. It is necessary first of all to remove from the scalp the scurf or any greasy scales that

may be present, as they tend to block the mouths of the hair follicles and provide a favorable soil for bacterial growth. During the first month of treatment the head should be frequently washed and anointed daily with an antiseptic ointment. The head should be shampooed every evening with a spirit soap lotion and then, after the hair has been thoroughly dried, the following ointment is rubbed carefully into the entire surface of the scalp:

R Acidi salicylici. gr. x (0.65 Gm.).
  Sulphuris præ-
    cipitati ..... gr. xxx (2 Gm.).
  Olei rosæ ..... ♏ ij (0.13 Gm.).
  Adipis benzo-
    atis .... ℥j (30 Gm.).
Misce. Ft. unguentum.

Drugs that should never be used when the hair is light or gray are: Resorcin, beta naphthol, empyroform, oil of cade, ichthyol, thiol, and tannic acid. Freshwater (Pract., Oct., 1913).

The frequency with which the scalp should be washed depends entirely upon the degree of oiliness of the scalp and hair. A greasy scalp requires more frequent cleansing than a dry one. In a general way it may be said that the scalp should be washed about once in two or three weeks. If the skin is very dry afterward, a pomade should be employed. **Soaps** containing **sulphur** and **tar** are useful. Some of the German superfatted soaps, especially one containing **sulphur, salicylic acid,** and **resorcin,** are particularly eligible for the purpose.

The drugs most successful in treating loss of hair are **euresol, bichloride of mercury, captol** and **chloral hydrate.** Temporarily one may expect good or very good response in 48 per cent. of men and in 56 per cent. of women. C. J. White (Jour. Amer. Med. Assoc., Sept. 24, 1910).

In premature baldness, **massage of the scalp** should be frequently and thoroughly done, for 20 or 30 minutes at a time. The masseur should use an emollient cream, such as:

R Ceræ albæ ... ℥vj (24 Gm.).
  Petrolei ...... ℥v (150 Gm.).
  Aquæ rosæ ... ℥iiss (75 Gm.).
  Sodii boratis . gr. xxxvj (2.4 Gm.).
  Sulphuris præ-
    cipitati ..... ℥vij (28 Gm.).
M. et ft. cremor.

Deep brushing with a long bristle brush for a few minutes night and morning is also advised, and **electricity** and **vibratory massage** have their advocates.

Pilocarpine is the only drug that appears to exert a specific action.

R Pilocarpinæ
  hydrochlo-
    ridi .... gr. xx (1.3 Gm.).
  Aquæ colonien-
    sis .... ℥iv (120 Gm.).
  Aquæ rosæ,
  Alcoholis ab-
    soluti ....āā ℥ij (60 Gm.).

M. Sig.: To be well rubbed in night and morning. G. T. Jackson and McMurtry (Med. Fortnightly, May 25, 1914).

Report of 3 years' experience with an **ultraviolet ray** quartz lamp utilizing 3½ amperes on a 220 direct current. Practically all forms of alopecia respond to it, even alopecia senilis showing favorable results and alopecia areata and trichophytina always responding rapidly. The distance from lamp to skin is 10 inches, and the initial time of exposure 15 minutes in blondes and 20 to 25 minutes in brunettes and gray persons. The younger the subject, the less the exposure. A given area can be treated but once a week, though with due local protection other parts can be treated on the same or following days. The eyes are protected by colored spectacles, and other exposed parts by zinc oxide plaster or 2 layers of towels. Hair that might obstruct the rays must be held away from the area to be treated, a bathing cap with appropriate windows being conven-

ïent. In recent cases a single treatment at times yields a cosmetic cure; in other patients a dozen exposures are required for satisfactory changes. Dieffenbach (Amer. Jour. Electrotherap. and Radiol., Sept., 1917).

In 25 cases observed by the writer, alopecia usually occurred 2 or 3 months after the onset of influenza, though occasionally during convalescence. It was generally of the diffuse type, although in 1 hospital case and 1 private case the lesions were patchy. In 21 cases the patients were females, but all were under 36 years of age. The aim should be to promote a healthy circulation of the scalp by **massage** with the head lowered; by **avoidance of obstruction to** the main **vessels** of supply to the scalp by padding the hat band, and by **stimulating lotions.** Ayres (Boston Med. and Surg. Jour., Apr. 24, 1919).

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ALOPECIA AREATA.—Alopecia circumscripta; area celsi.

DEFINITION.—Alopecia areata is a disease of the hairy system characterized by the more or less sudden occurrence of round or oval circumscribed bald patches, in rare cases coalescing and producing total baldness.

SYMPTOMS. — The disease is usually limited to the scalp. The patches are circumscribed and round, and vary in size from a coin to the palm of the hand. The skin is smooth, soft, of a dead-white color, and totally devoid of hair. Occasionally the patches are pinkish as a result of slight hyperemia. The follicular openings are contracted and less prominent than in the healthy scalp.

To the feel the skin is thin, soft, and pliable. In the beginning, the patches are level or slightly ele-

vated, while later they are sometimes slightly depressed.

The course of the disease is extremely variable. In some cases the bald patches develop suddenly in the course of a few hours. In other cases, the hair loss is gradual, extending over a period of a few days or weeks. The areas then spread by peripheral extension until they reach

Alopecia totalis following an ordinary alopecia areata. (*Schamberg.*)

a certain size, when they remain stationary.

In some cases the entire scalp becomes denuded of hair, giving to the patient a most grotesque appearance. In extensive cases it is by no means rare for the eyebrows and eyelashes to be lost. In men the bearded region of the face may be involved, either alone or in conjunction with the scalp.

The duration of the disease varies

greatly. Recovery seldom occurs in less than a few months, while many cases last several years. The disease may occur at any period of life. In young individuals the hair usually returns sooner or later. In adults, the baldness may persist and prove refractory to all treatment.

When regrowth occurs, the patch is first covered by fine, downy, whitish

Alopecia areata. *Schamberg*.

hairs which are either shed or later converted into coarse and pigmented hairs. Not infrequently the hair grows in and the patient thinks he is on the road to recovery, only to have his hopes shattered by the hair falling out again. As a rule, there are no subjective symptoms to be observed in such cases.

Alopecia areata occurs with similar frequency in the two sexes. It is more common in youth and early adult life than in other age periods.

Crocker states that, of 506 hospital cases, 214 were under 15 years of age, and 214 occurred in persons between the age of 15 and 35.

ETIOLOGY.—There are two distinct theories of the causation of alopecia areata. One school insists that the disease is parasitic, and cites occurrences of epidemics in institutions as proof of this view. Epidemics have been observed chiefly in France and Germany: Bowen and Putnam have also published the details of an outbreak in an institution in this country.

The cause of alopecia areata is not an infection, but some neurotrophic influence. Division of the second cranial nerve experimentally causes it; besides, thallium acetate applications cause neurotrophic affections of the entire body. And with atrophy of the fibers of the sympathetic nerves in certain regions alopecia results, especially when the trigeminus is affected. From his observations the writer believes alopecia areata always to be neurotrophic in character. E. Richter (Berl. klin. Woch., Dec. 29, 1902).

Alopecia areata is trophoneurotic in origin, as first urged by Jacquet, who noted some close relation between alopecia and dental neuralgia. His investigations show that neuralgia occurs before, with, or after the alopecia, in almost all cases. This dental theory of the origin of alopecia is confirmed by a case-history which the writer quotes, a child in whom the condition disappeared after the affected gum had been cauterized. F. Trémolières (Presse méd., June 14, 1902).

Recalling Jacquet's theory that baldness is of nervous origin, and is connected with skin diseases, dental troubles, and crises of gastrointestinal and other origin, the writer refers to a case in which the cure of a fistula in ano, complicated with entire loss of hair, was succeeded by

complete restoration of eyelids, eyebrows, and hair of the scalp. Eyraud (Presse méd., Mar. 30, 1904).

There exists a more or less intimate and obvious relationship between genital disturbances and this disorder. In the female sex there is a form of alopecia that follows the menopause and even a prolonged suppression of the menses. Such alopecia may be either mild or severe. This disease may also follow oöphorectomy, and here again the prognosis is variable. In less frequent instances alopecia appears, usually in a mild form, in the course of several consecutive pregnancies. R. Sabouraud (Annales de dermat. et de syphil., Feb., 1913).

Instance in an Italian boy, 5 years old, of ringworm of the scalp and alopecia areata appearing simultaneously in the same location. He deemed it of some interest on account of its possible bearing on the cause of some of the epidemics of alopecia areata occasionally reported. J. E. Lane (Boston Med. and Surg. Jour., Jan. 11, 1917).

Illustrations of the teeth of persons with alopecia areata. Some initial teratologic disturbance is responsible for the tendency for the hair to fall out, and for the defective teeth and defective growth of teeth and nails. Inherited syphilis is sometimes but not always responsible. Sabouraud (Presse Méd., Aug. 23, 1917).

On the other hand, there is irrefutable clinical evidence of the neuropathic origin of cases of alopecia areata. Nervous shock, such as fright, prolonged anxiety, etc., and traumatism to the scalp have been directly followed by areate loss of hair.

[I recently saw a boy admitted to the Polyclinic Hospital for the fracture of the skull who developed alopecia areata before leaving the institution. Max Joseph has produced the disease in cats by excision of the second cervical ganglion. J. F. S.]

It would, therefore, appear that there are two varieties of alopecia areata, the one parasitic and the other trophoneurotic. In the epidemic observed by Bowen and Putnam, the patches were not identical with those commonly observed, but were smaller and more irregular in shape. Some of the English dermatologists are of the opinion that alopecia areata is prone to occur in those who have at some previous period suffered from ringworm of the scalp.

Stimulating and antiparasitic remedies give the best chance of success in this affection, and in early cases there is a fair prospect of arresting the disease. The hair obtains its nutrition from the papilla, and the difficulty of reaching the deeper parts of the hair-follicle by external application must be borne in mind. The best remedies are probably those which keep the skin of the patch in a state of slight permanent irrigation, and this object may be obtained by the daily application of moderately strong irritants, such as tincture of iodine, lactic acid, acetic acid, chrysarobin, sulphur and mercurial ointments. The author has found (1) the B. P. **unguentum hydrargyri iodidi rubri** (diluted from 4 to 2 per cent.); (2) the **unguentum hydrargyri oxid: rubri**, with **acetum cantharidis**, 3j to 3j (4 to 30 Gm.), and (3) equal parts of **sodium chloride** and **petrolatum**—used for the treatment of ringworm—serviceable for their antiseptic and stimulating properties. S. E. Dove (Clin. Jour., Jan. 21, 1914).

The great French dermatologist, Sabouraud, regards his microbacillus as the probable cause of alopecia areata, though the influence of syphilis is not overlooked by him.

In a review of current theories—the parasitic, the neurotrophic, and the reflex irritation theory of Jacquet—the writer dismisses them all. In some families it is hereditary. It occurs not infrequently in connection

with vitiligo and exophthalmic goiter. It is common in women at or about the menopause. Apart from these groups a large number of cases, at least in childhood and adolescence, are due to syphilis inherited in a larval form, a view fortified by excellent results obtained with mercurial treatment. R. Sabouraud (Ann. de Derm. et de Syph., Ser. 6, i, 177, 1920).

PATHOLOGY. — Both Giovanni and Robinson found evidences of inflammatory disturbances, chiefly in subpapillary layer. Perivascular cell infiltration was observed in both early and late lesions. Subsequently atrophic changes take place with destruction of the hair papillæ.

The characteristic hair of alopecia areata has the shape of an exclamation point. The upper part is pigmented and normal, while the lower portion is atrophied and without pigment. Sabouraud describes an ampullar swelling (*the peladic utricle*) filled with the microbacillus in the upper third of the hair follicle.

adults the prognosis is usually favorable, while in advanced adults it is unfavorable. The longer the disease has persisted, the more unfavorable is the prognosis. The duration of the disease is uncertain and relapses are not uncommon.

TREATMENT.—The internal treatment consists of the use of such tonics as iron, strychnine, quinine, codliver oil, phosphorus, and arsenic. Duhring considers arsenic to be "especially serviceable."

The local treatment has for its purpose the stimulation and rubefaction of the scalp with the object of increasing the blood-supply to the follicles. Many cases terminate in spontaneous recovery, and conservative judgment is desirable in interpreting the value of remedies employed. Among the many medicaments which have been advised are alcohol, cantharides, capsicum, the essential oils, turpentine, carbolic acid, trikresol, ammonia, sulphur,

ALOPECIA AREATA.	RINGWORM.
1. Rapid onset.	1. Slow, insidious onset.
2. Patches are :—	2. Patches are :—
(*a*) Totally devoid of hair.	(*a*) Covered with broken-off stumps.
(*b*) Pale or whitish in color.	(*b*) More or less reddened.
(*c*) Smooth or soft.	(*c*) Rough and scaly.
(*d*) Follicles contracted.	(*d*) Follicles prominent; "goose-flesh" appearance.
3. Absence of fungus.	3. Trichophyton fungus present.
4. Common in adolescence and adult life.	4. Occurs almost exclusively in childhood.

The baldness of early syphilis may bear some resemblance to alopecia areata. Apart from the presence of other evidences of the disease, the patches are moth-eaten in appearance and not sharply circumscribed. The surrounding hair and scalp are lusterless and dirty, whereas in alopecia areata they are perfectly normal.

PROGNOSIS.—In children recovery usually takes place. In young

iodine, mercury, chrysarobin, betanaphthol, etc.

The following lotion will be found of value :—

R Tinct. cantharides,
    Tinct. capsici, of each f℥iss (6.00 c.c.).
    Ol. ricini .... f℥ij (8.00 c.c.).
    Aquæ cologniensis . f℥j (30.00 c.c.).
Sig.: Brush in vigorously each day.

Instead of lotions, ointments such as the following may be employed :—

℞ *Betanaphtholis* .... ʒj (4.00 Gm.).
Vaselini .... ʒj (31.00 Gm.).
Ol. bergamot. .... ♏ xl (2.46 c.c.).
    Sig.: Rub in twice a day.

An efficient treatment consists in the swabbing of the bald areas once or twice a week with

℞ *Phenolis,*
    Alcoholis, of each..... fʒss (15.00 c.c.).

Or, 50 per cent. **trikresol** may be employed.

Within recent years I have employed a **chrysarobin ointment** which has given me more uniformly good results than any other topical application:—

℞ *Chrysaro-*
    bini ...... gr. x-xxv (0.65-1.62 Gm.).
    Lanolini .... ʒj (4.00 Gm.).
    Adipis benzo-
    inati ...... ʒvij (27.21 Gm.).

M. Rub in in small quantity. Protect the eyes from contact with ointment.

> Case of a young girl in which there was a circular patch three inches in diameter on the scalp at the side of the occiput, hairless, smooth, and shining. The treatment consisted in painting it with a 30 per cent. solution of **formaldehyde.** This was done every day for the first week or two, until signs of inflammatory reaction appeared. The treatment was then suspended, and a sedative ointment applied. When the inflammation subsided the formaldehyde was again continued, stopping the application as soon as inflammatory trouble appeared. This routine of treatment was persevered in for about six or nine months. About this time a growth of hair made its appearance, continued to grow, and in every way corresponded with the surrounding hair. One year after cessation of treatment the growth of hair was continuing in a perfectly normal way. J. J. McInerny (Brit. Med. Jour., Jan. 25, 1908).

> The writer deems it a great mistake to treat the patch of alopecia alone; the aim should be especially to prevent the development of new patches. Another error is to wait to see whether the alopecia will subside; it is better to treat it from the first as if it were going to be a grave form. He advises to brush the entire scalp with a hard toothbrush dipped in a tonic and irritant mixture. His formula for this is: cologne water, 300 c.c. (10 ounces); **glacial acetic acid,** 10 Gm. (2½ drams), and commercial solution of **formaldehyde,** 1 Gm. (15 grains). A lotion of 30 Gm. (1 ounce) of **Hoffmann's fluid** with 1 Gm. (15 grains) of glacial acetic acid is applied to the patch itself and its vicinity. In case the course of the alopecia seems threatening rapid extension, the small hairs broken off 3 or 4 mm. above the skin, he resorts to a **cade oil salve.** Men rub it in every evening and wash it out with soap in the morning; women three times a week with a weekly soap shampoo. The general health improves under **mercurial treatment,** as well as the alopecia; the writer's success in this line has been so striking that he advocates mercurial treatment for young people with poor health or vague disturbances even if the idea of syphilis seems preposterous. When the alopecia develops at the menopause, **ovarian treatment** may aid, but spontaneous recurrence of hair is often observed. R. Sabouraud (Presse méd., Dec. 4, 1920).

The **faradic current** applied with a wire brush electrode is often useful, as is likewise the use of **high-frequency currents.** In obstinate cases blistering of the affected areas may be resorted to.

PHOTOTHERAPY.—Many writers, including Finsen, Hyde, Montgomery, Kromeyer, and others, have testified to the value of **actinic light rays** in this disease. It is admitted that many cases in which light is used might have recovered spontaneously. Kromeyer's results, however, in cases

of extensive and even total alopecia of years' standing indicate that light therapy is one of the most useful measures in the treatment of this disease.

The iron arc or carbon arc may be employed. The ordinary London Hospital type of lamp suffices for this purpose and permits of the exposure of a surface area of the size of a silver dollar.

Reaction varying in degree from an erythema to the formation of a blister results at the end of some hours. The same area can be again treated after the expiration of two or three weeks.

> Severe case of alopecia areata, rebellious alike to applications of mercury bichloride, pilocarpine, croton oil, etc., as well as to the use of a constricting band and to internal medication, in which exposures of the affected areas to the **ultraviolet rays,** by means of Kromeyer's lamp, gave good results. These rays induce pronounced and prolonged cutaneous hyperemia. They are both more active and safer than the X-rays. R. Horand (Lyon méd., Aug. 18, 1912).

> The **ultraviolet rays** have given excellent results in the writer's hands in cases of alopecia areata and other dermatoses. A. Fischkin (Ills. Med. Jour., May, 1916).

> The **quartz lamps** (Kromayer and Alpine) are cleanly and convenient agents for the treatment of alopecia areata. The results in 50 cases, though not brilliant, were at least satisfactory. More than half of the patients were followed to complete recovery, while in 78 per cent. of the cases the new hair had at least begun to grow. Fox (Med. Rec., Nov. 27, 1920).

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ALSOL. See ALUMINUM: ALUMINUM ACETOTARTRATE.

ALUM (*Alumen*).—The alum used in medicine is, chemically, the double sulphate of aluminum and potassium [$AlK(SO_4)_2 + 12H_2O$]. It occurs in large, octahedral, translucent crystals, or as a colorless powder, odorless, but with a sweetish, strongly astringent taste. When left in an open bottle, the salt becomes whitish on the surface, owing to the absorption of ammonia from the air. Dried, "burnt," or exsiccated alum (*Alumen Exsiccatum*), i.e., alum from which the water of crystallization has been driven out by heating, occurs as a white, granular, strongly hygroscopic powder.

DOSE.—The dose of alum for internal use (rarely employed) is 5 to 30 grains (0.03 to 2.0 Gm.); the average dose is 7½ grains (0.5 Gm.). To secure an emetic effect, 1 to 2 drams (4 to 8 Gm.) must be given.

MODES OF ADMINISTRATION.—Alum is soluble in 9 parts of cold water (the saturated solution thus containing, roughly, 10 per cent.), and in 0.3 parts of boiling water. It is completely insoluble in alcohol, but dissolves readily in warm glycerin. Dried alum, possessing greater concentration than the crystalline form, requires more water for dissolution—17 parts of cold and 1.4 parts of boiling water. When exhibited for other purposes than as an emetic, alum is best given in a flavored syrup, *e.g.,* syrup of orange peel. When it is used to secure emesis, a small amount of simple syrup may be employed as vehicle. The subsequent ingestion of warm water augments its emetic effect. For astringent gargles, sprays, anhydrotic lotions, and rectal or vaginal injections, solutions containing 2½ to 20 grains (0.15 to 1.2 Gm.) of alum to the ounce (30 c.c.) of water should be prescribed. When an astrin

gent eye-wash is desired, 2 or 3 grains (0.12 to 0.20 Gm.) of alum to the ounce of water may be used. The "alum curd," made by adding to a pint (473 c.c.) of milk 2 drams (8 Gm.) of alum, boiling the mixture, and straining off the curd, is also a useful preparation for this purpose. Dried alum, being anhydrous, is especially adapted for use as a dusting powder, for insufflation, and in ointments. It is applied to superficial growths as an escharotic. A glycerite of alum is official in the British Pharmacopœia.

INCOMPATIBLES.—The salts of aluminum, including alum, are incompatible with the alkalies and carbonates of the alkali metals; with the tartrates; with tannic acid, and with salts of iron, mercury, and lead.

CONTRAINDICATIONS.—In individuals subject to bronchial irritation, the long-continued use of alum is inadvisable, in view of the exciting effect it exerts on these structures.

PHYSIOLOGICAL ACTION.—When applied externally alum causes hardening of the skin, or, if used in concentrated solution, exerts a slight caustic effect. Whenever it is brought in contact with albumin, as occurs when it is applied to a denuded area, the albumin is coagulated. The precipitate is soluble, however, if an excess of albumin be present.

The familiar *astringent* and *antiseptic* effects of alum and other aluminum salts depend upon this coagulating property. Their power of penetrating into tissue-cells is, however, very limited according to Siem. Yet it is very effective when hemorrhage for instance is of capillary origin.

Small doses of alum taken orally at first stimulate the flow of saliva, then reduce it through their astringent ef-

fect. The buccal mucosa becomes whitish and shriveled, owing to coagulation of the albuminous constituents, and the enamel of the teeth is likely to crack in places. On reaching the stomach, the drug causes a decrease in the amount of gastric juice secreted, and coagulates the pepsin. A similar effect being exerted in the intestinal canal, constipation results. In larger doses, the *emetic* effect of alum becomes manifest, and a *purgative* effect may also be noted, irritation succeeding the preliminary astringent effect.

UNTOWARD EFFECTS AND POISONING.—The injurious effect of alum on the teeth may be avoided (1) if care be taken to cleanse them well at once after employing an alum gargle or mouth-wash; (2) by limiting the use of alum to applications of a strong solution or of the solid salt in all cases in which local astringent effects will suffice. The unfavorable action of alum when long employed by persons subject to bronchial irritation has already been referred to.

> The influence of alum in baking powders was studied by a Referee Board of Consulting Scientific Experts composed of R. H. Chittenden, A. E. Taylor, and J. H. Long, appointed by the U. S. Department of Agriculture. The general conclusion reached was that alum baking powders are no more harmful than any other baking powders, but that it is wise to be moderate in the use of foods that are leavened with baking powder. (Bulletin No. 103, Apr. 29, 1914).

Large amounts of alum taken internally cause nausea, vomiting, pain in the abdomen, and diarrhea, owing to the inflammation of the gastrointestinal mucosæ produced through the cellular albumins.

Case in which, through gargling with a concentrated alum solution, a portion of the fluid was accidentally swallowed. This was followed by severe abdominal pains, vomiting of mucus and blood (39 times), and voiding of blood-stained urine. Recovery only after the lapse of thirteen days. Kramolin (Therap. Monatsh., 325, 1902).

Alum baking powders and pastry to which alum has been added in order to whiten the product are possible sources of gastrointestinal irritation, though the amount of aluminum liberated, at least in the case of bread baked with alum powders, is often so slight as to be of doubtful importance.

THERAPEUTIC USES.— As an Astringent.—This is the chief use of alum. Combined with it is an antiseptic effect, which is also of value.

In all catarrhal and relaxed states of the mucous membranes, as well as in certain skin affections, alum is beneficial when locally applied. Aqueous solutions of from 5 to 20 grains to the ounce (1 to 4 per cent.) strength are chiefly employed; stronger solutions induce undesirable secondary irritation.

In **catarrhal throat affections** fluid preparations containing alum (1 to 5 per cent.) form a useful gargle or spray. Since alum is injurious to the teeth, the mouth should be washed out, preferably with some alkaline solution, after using this drug. A glycerite of alum (10 to 20 per cent. solution of alum in glycerin, the preparation of which is greatly facilitated by heating) is very efficacious when applied locally in **subacute pharyngitis** and **laryngitis,** especially where a tendency to edema of the tissues involved is present. For the relief of **hoarseness** or of **tickling sensations** in the throat, a mixture of equal parts of powdered alum and sugar, placed

on the tongue and allowed slowly to dissolve, is productive of benefit (Bunnell).

In **acute coryza** alum has been incorporated in snuff, to which it imparts astringency. The following preparation is suitable for use in the early stages of coryza:—

℞ *Alum* .... 3 grs. (0.2 Gm.).
  Morphine sulphate . 2 grs. (0.13 Gm.).
  Cocaine hydrochlo-
  ride .... 1 gr. (0.065 Gm.).
  Camphor,
  Bismuth ....of each 2 drs. (7.77 Gm.).
M. bene. Sig.: To be used as snuff every two hours; a small quantity in each nostril.

In **follicular tonsillitis** and **diphtheria** alum in pencil form may be applied to the involved surfaces with benefit.

In **conjunctivitis** alum may also be used. A 0.5 per cent. solution may be used as a lotion, or the alum curd, made by the addition of powdered alum to milk or white of egg until a curdy mass is formed, may be applied to the eye every two hours. Similar applications prove effective in **ecchymosis of the eyelid** (black eye). In **gonorrheal ophthalmia** alum has also been used in a solution containing 6 grains of the salt in 1 ounce of water, applied four times daily. In **granular conjunctivitis** a crystal of alum may be drawn over the involved mucous surface after turning the lid (Bunnell).

In salivation or **ptyalism** of mercurial origin a 4 per cent. solution of alum may be employed for its astringent action.

In the treatment of **night-sweats,** or in sweating of the hands and feet (**hyperidrosis**), washing the skin surfaces with a 0.5 per cent. solution of alum will markedly improve the condition.

In **chilblains** a 4 per cent. solution of alum has been applied with benefit.

In **gonorrhea** and **leucorrhea** alum has been used as an astringent injection or douche in ½ to 2 per cent. strength.

In **pruritus vulvæ** a 4 per cent. solution of the salt will not infrequently relieve the itching.

In **ingrowing toenail** with granulations absorbent cotton soaked in a 6 per cent. solution of alum may be introduced under the edge of the nail.

In **chronic dysentery** a 1 per cent. solution of alum is sometimes employed as a rectal injection.

As a styptic alum is likewise an effective agent.

In **epistaxis** it will often act promptly. Pledgets of cotton should be dipped in a saturated solution of alum and packed in the bleeding cavity; they may be left in until all danger of recurrence has passed—generally about twelve hours. In minor degrees of hemorrhage the alum solution may be sprayed in, or powdered alum may be used as snuff or introduced by means of an insufflator.

Similarly, in hemorrhage succeeding upon the **extraction of teeth**, the placing in the cavity of cotton dipped in a saturated solution, or the introduction of powdered alum, will often be effective in arresting the bleeding.

In **hemoptysis** a fine spray of 5 per cent. alum solution is claimed to have been productive of benefit.

In the **intestinal hemorrhage of typhoid fever** alum has been recommended by many clinicians, Whitla in particular. It is believed to do good in this condition through its antiseptic properties, as well as through its astringency.

In **uterine hemorrhage** of all kinds alum is a useful styptic. It may be employed as an injection in the strength of 1 dram to the pint, or, as R. Beverly Cole recommended, an egg-shaped piece of alum may be inserted into the uterine cavity. Not only is the styptic effect produced, but the tissues of the uterus are stimulated and the organ is caused firmly to contract.

As a Caustic.—Dried ("burnt") alum, which exerts an escharotic effect, owing to the fact that in addition to the inherent properties of alum it withdraws water from the tissues, may be applied to **exuberant granulations, condylomata, chronic conjunctival inflammations,** etc.

Burnt alum may also be used as a dressing for **sluggish ulcerations** and as an application to **swollen gums** and in **ulcerative stomatitis** (Bunnell).

As an Emetic.—In doses of 1 or 2 drams alum has been used as an emetic, especially in the treatment of **croup** in children. A teaspoonful of the salt may be dissolved in 6 tablespoonfuls of a mixture of syrup and water, equal parts, and administered every fifteen minutes.

This sometimes serves quickly to arrest an impending attack of croup, the astringent effect of the salt upon the mucosa of the throat contributing in the benefit by counteracting the local hyperemia.

As a Stimulant to Peristalsis.—In doses of ½ dram every four hours alum has been found to induce purgation. The large amount of watery fluid thrown out from the mucosæ in the presence of alum apparently obviates its irritating influence on these membranes. In **tympanites** due to peri-

toneal **inflammation** succeeding upon abdominal operations in cases suffering from infective states of the abdominal viscera, the high rectal injection of an ounce of alum in a quart of water has been found effectively to excite contractions of the paretic gut.

> Case in which Epsom salt, calomel, soap and water, castor oil, glycerin, turpentine, and oxgall were successively used without avail. A solution of an ounce of powdered alum in a quart of warm water was injected into the rectum, and in ten minutes flatus escaped from the rectum. In an hour the enema was repeated successfully. The patient was practically convalescent on the following day. Since this case, the author has used the alum enema in hundreds of cases, and always with good results. Sometimes it is necessary to repeat the injection before it will act, and this can be done with safety an indefinite number of times.
>
> There is sometimes some pain, not severe, attending its use. Injected like any other enema, probably in no instance does it go above the sigmoid flexure. The throwing off by the bowel of a tubular cast is of no importance, as it is composed simply of mucus whose albuminous elements have been coagulated by the alum.
>
> The alum seems to have as specific an action in inducing intestinal peristalsis as has castor oil when taken into the stomach. It does not produce a serous exudation from the intestinal walls, and for that reason the author prefers it to Epsom salt when the stomach will retain it. During nine years in which alum enema was used, percentage of mortality in abdominal work has been a little less than one-half of what it was during the preceding seven years. Hardon (Amer. Jour. of Obstet., June, 1901).

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ALUMINUM (*Aluminium*). — A bluish-white, silvery metal, noted for its low specific gravity (2.7) and its unalterability on exposure to the air.

The most important of the compounds of the metal aluminum employed in medicine, viz., the double sulphate of aluminum and potassium, has already received separate consideration (*v*. Alum). Numerous other salts have been used, chiefly externally, as astringents and antiseptics.

Taken internally, the salts of aluminum are, according to some observers, not all absorbed from the gastrointestinal tract, this accounting for the fact that no functional disturbances in the organism at large occur as a result of their ingestion. According to others, however, alum (and probably other salts) is absorbed, in extremely small amount, in the alimentary canal, and is eliminated with the bile and urine. When administered experimentally to animals by subcutaneous injection, soluble salts of aluminum cause no symptoms at all until several days or even weeks later (Siem), when the metal is no longer present in the circulation. In mammals the symptoms appear in from three to five days, and are in many ways similar to those of subacute arsenic poisoning. The animal shows loss of appetite, obstinate constipation, emaciation, and languor. Next there appears vomiting. Voluntary movements, executed only upon coercion, are attended with trembling and twitching. Sometimes there is general tremor or convulsive twitching, and sometimes extreme weakness or partial paralysis of the posterior limbs. There is complete loss of sensibility to pain, though consciousness is retained. Finally, control of the tongue and the power

of swallowing are completely lost, saliva dribbling from the mouth. The symptoms correspond precisely to those of human acute bulbar paralysis. Such phenomena never result from the oral use of aluminum salts, even where long continued (Sollmann). Diarrhea and albuminuria appear before death. On post-mortem examination the gastrointestinal mucosæ are found hyperemic and swollen, and the kidneys and liver frequently show fatty degeneration, the former presenting, in addition, cortical hemorrhages.

> When aluminum vessels were first used for cooking some doubt existed as to their safety. Increasing experience has shown that such objections do not exist. The writer observed that the largest amount of aluminum was detached when marmalade was made with oranges and lemons, but the amount recovered was so small that it would have been perfectly harmless even if the entire 2½ ounces of preserves had been eaten at one meal by a single individual. John Glaister (Editorial Therap. Gaz., Sept., 1913).

> When aluminum, in the form of aluminum lactate or sodium aluminum lactate, is fed to rabbits, cats, or dogs for long periods of time, certain distinct effects such as diarrhea, with, at autopsy, corrosion of the stomach, together with congestion, and a hemorrhagic condition of the intestinal mucosa result. Large doses caused numerous areas of intestinal hemorrhages and a few areas of ulceration, which were especially marked in the large intestine. Roth and Voegtlin (Jour. Pharm. and Exper. Therap., Feb., 1916).

Following are some of the more important salts of aluminum employed in medicine :—

Aluminum Hydroxide (*Alumini Hydroxidum*), $Al(OH)_3$, made by precipitating a soluble salt of aluminum with an alkali or alkaline carbonate. It occurs as a light, amorphous, colorless, tasteless powder, soluble in acids and alkalies. It is used as an astringent in **inflammatory skin affections**.

Aluminum Sulphate (*Alumini Sulphas*), $Al_2(SO_4)_3 + 18H_2O$, prepared from the hydroxide by dissolving it in dilute sulphuric acid. It occurs as a white, crystalline powder or in larger crystals or pencils, and, like alum, has a sweetish and astringent taste. It is freely soluble in water, and has been used for much the same purposes as alum itself, viz., as an astringent, antiseptic, and caustic in the treatment of affections of the nose and throat, including **enlarged tonsils** and **nasal polypi**; of the uterus, including **endometritis**; as a lotion for **foul ulcers**, and in vaginal conditions associated with offensive discharges. The strength of the solutions used is the same as with alum.

The following aluminum compounds are non-official :—

Aluminum Acetate (basic), $Al_2O, 4C_2H_3O_2 + 4H_2O$. Obtained in solid form from its solutions by rapid drying on glass at a low temperature, this salt occurs as a colorless, crystalline or amorphous powder which is insoluble in water. It is antiseptic and astringent, and has been used internally in **dysentery** in doses of 5 to 10 grains (0.3 to 0.6 Gm.). An 8 per cent. solution of aluminum acetate is known as "liquor Burowii," which has been extensively used as an application in **skin affections**, and in **suppurating wounds**. One to 3 per cent. solutions are useful as a mouth-wash, and are particularly effective in overcoming **fetid breath**. In a solution of

1 to 150 strength, this salt of aluminum may be used as an astringent enema in affections calling for such a measure.

Usefulness of aluminum acetate solution emphasized. For certain surgical purposes this is one of the best antiseptic solutions, though it is unknown to most surgeons and practitioners. **Burns** may be treated with dressings wetted with a 1 per cent. solution of aluminum acetate. This solution, while antiseptic, is also non-toxic, non-irritant, and yet markedly astringent. It is not to be employed in surgical operations, as it spoils steel instruments; but as an antiseptic for moist fomentation of **wounds** that are **infected** or probably unclean, or as a medicament for a bath in which to place an infected hand or foot for continuous irrigation, it is to be strongly recommended. The common strength is that of 1 dram of the liquor aluminii acetatis of the German Pharmacopœia (a 7½ per cent. solution) to 1 fluidounce of water. There is no danger of poisoning from it. By the employment of continuous irrigation by means of a bath of the 1 per cent. solution, pyogenically infected hands and feet, which but for the action of the solution would have called for amputation, have been saved. For **dermatitis,** whatever its cause; for **suppurating open wounds,** and for cutaneous **erysipelas,** much is to be said for the favorable results obtained. One objection that should be mentioned is that after three weeks of continuous irrigation of a member such as the hand the surface tissues may assume a ligneous hardness. M. F. Waterhouse (Hospital, Aug. 27, 1910).

The writer observed 3 cases in which dressings with solution of aluminum acetate produced necrosis of the injured hand. The effect of the dressing was similar to the burns caused by phenic acid. Esau (Med. Klinik, July 14, 1912).

Aluminum Acetotartrate (Alsol), prepared by mixing a 5 per cent. solu-

tion of basic **aluminum acetate with** a 2 per cent. solution of tartaric acid and evaporating to dryness. It occurs in colorless crystals, or in whitish amorphous masses having a slightly acid, astringent taste. It dissolves slowly, but completely, in water, but is insoluble in alcohol and ether.

This substance has an action similar to that of aluminum acetate, and is one of the best of the aluminum salts used in medicine. It has been employed largely, though not exclusively, in **diseases of the respiratory passages.** Thus in 0.05 to 2 per cent. solutions it has been used as a nasal douche. Mixed with 2 parts of powdered boric acid it may be used as a snuff. In **tonsillitis** a 1 per cent. solution of it makes a suitable gargle. Strong solutions (*e.g.,* 50 per cent.) have been employed with advantage in the treatment of **chilblains and skin diseases** of various kinds—also in **wounds** as disinfectants. Eye affections, such as **ophthalmia neonatorum, chronic** types of **conjunctivitis,** etc., have also been treated with this salt.

Solution of aluminum acetate is more efficacious than the commoner applications, iodine, ichthyol, lead and opium, etc., in the treatment of local congestions such as **boils, carbuncles,** and especially in facial **erysipelas.** He has used it also with marked success in severe **cellulitis and inflammatory rheumatism** and declares it the best remedy for **ivy poisoning.** Several thicknesses of gauze are soaked with the solution and applied to the part, covered with rubber tissue or oiled silk, and a bandage applied. It need be renewed only once or twice in 24 hours. Liquor alumini acetatis of the National Dispensatory is the best solution, and is made up as follows: Aluminum sulphate (N. S. P.), acetic acid (N. S. P.), of each, 300

Gm. (10 ounces); calcium carbonate (C. P.), 130 Gm. (4⅓ ounces); distilled water, 1000 c.c. (1 quart). Stansbury (Amer. Jour. of Surg., Feb., 1912).

Aluminum Boroformate, prepared by saturating with freshly precipitated and well-washed aluminum a solution of 2 parts of formic acid and 1 part of boric acid in 6 or 7 parts of water. It occurs in pearly scales, which are hygroscopic and dissolve completely, though slowly, in water. Its solution has a sweet, faintly astringent taste, and does not coagulate solutions of albumin. Martenson in 1894 recommended this salt strongly for use as a gargle in the **throat affections in children,** preferring it to all other preparations of aluminum, partly owing to its relatively pleasant taste.

Aluminum Borotannate (Cutal), a product of the reaction of tannic acid with borax and aluminum sulphate. It is a brownish insoluble powder, which combines with tartaric acid to form **Aluminum Borotannotartrate** (soluble Cutal).

This salt, in common with the other aluminum compounds, is antiseptic and astringent. It has been used chiefly in skin affections and is recommended particularly in **weeping eczema** and **pruriginous** affections. The following formula may be employed:—

R. *Aluminum boro-*
tannate .... 1 dr. (4 Gm.).
Olive oil .... 2½ drs. (10 Gm.).
Lanolin..to make 10 drs. (40 Gm.).

When the flow of secretions has been arrested, the drug may be used with advantage as a dusting powder and astringent in the following mixture:—

R. *Aluminum boro-*
tannate,
Zinc oxide,
Powdered talc, of
each .... 2½ drs. (10 Gm.).

In **hemorrhoids** Koppel has recommended the use of an ointment containing 10 per cent. of cutal, and in **fissures** of the hands of one formulated thus:—

R. *Cutal* .... ¾ dr. (3 Gm.).
Oil of sweet alm-
onds,
Lanolin ..of each 3¾ drs. (15 Gm.).
Orange-flower
water .... 2½ fl. drs. (10 Gm.).

Aluminum borotannotartrate, or soluble cutal, has been used in the treatment of **second-degree burns,** as a 10 per cent. solution in glycerin in **follicular throat affections,** in **catarrhal metritis,** in **hemorrhoids,** and in **gonorrhea.**

Aluminum Borotartrate (Boral), a combination of aluminum, boric acid, and tartaric acid. It occurs as white crystals having a sweetish, astringent taste, and is freely soluble in water. It is useful in **inflammatory diseases** of the **nose** and **nasopharynx,** in **erysipelas,** and, in solution with tartaric acid, has given good results in **gonorrhea.** It may be employed either alone in watery solution or in glycerinated mixtures.

Aluminum Carbonate, $Al_2(CO_3)_2$, occurring in chalky-white, easily powdered, tasteless masses. According to Gawalewski, it constitutes an extremely mild styptic and astringent, and is hence better adapted than are burnt alum and other aluminum preparations in the treatment of various **ocular affections, croup, diarrhea, hemoptysis, skin eruptions,** and **hyperidrosis.**

Aluminum Chloride, $Al_2Cl_6 + 12$-H_2O, a yellowish granular, crystalline, hygroscopic powder, soluble in water, alcohol, and ether. It has been used internally in **tabes** in doses of 1½ to 4 grains (0.1 to 0.25 Gm.), and externally as a disinfectant.

Aluminum Phenolsulphonate (Sulphocarbolate), $Al_2(C_6H_4HSO_4)_6$, a reddish powder with weak phenol-like odor and a strongly astringent taste, soluble in water, alcohol, and glycerin. It has been recommended as a substitute for iodoform in the treatment of **superficial, circumscribed, suppurating lesions,** and of **cystitis.**

Aluminum Salicylate, $Al(C_6H_4$-$OHCOO)_3$, a reddish powder, insoluble in water and alcohol, soluble in alkalies. Used as an antiseptic powder for insufflation in **catarrhal states** of the **nasal** and **pharyngeal** mucous membranes, and in **ozena.**

Aluminum Silicate, $Al_2Si_3O_9$, a white substance, insoluble in water and acids. It has been recently recommended in the treatment of **gastric hyperacidity** and **hyperesthesia.**

Investigations of the action of silicate of aluminum upon the gastric secretions and upon disease symptoms resulting from abnormalities of secretion. Under the name *neutralon,* this substance occurs as a fine, tasteless, odorless, and insoluble powder. Taken into the stomach it reacts with the excess of hydrochloric acid to form silicic acid and aluminum chloride. The latter acts as a protective and astringent to the gastric mucosa in a manner similar to silver nitrate and bismuth, and has no toxic effect. In all cases of **hyperacidity** or **hypersecretion,** whether of neurotic origin or due to organic disease or injury, the remedy was found to be very effective in reducing the acidity, relieving pain, and aiding digestion. Results especially good in persistent cases of hypersecretion with motor insufficiency. **Gastric hyperesthesia** associated with **anemia** and **chlorosis** favorably influenced in several instances. **Excessive acidity** in cases of **gastric ulcer** was also reduced. The drug was given in doses of ½ to 1 teaspoonful in 3 ounces of water, one-half to one hour before meals. No untoward symptoms. Rosenheim and Ehrmann (Deut. med. Woch., Jan. 20, 1910).

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ALUMNOL, the aluminum salt of betanaphthol-disulphonic acid $[Al_2(C_{10}H_5OH(SO_3)_2)_3]$, is made by adding a solution of barium naphthol-disulphonate to one of aluminum sulphate, filtering off the precipitate of barium sulphate, and evaporating to dryness. It contains about 5 per cent. of aluminum, and occurs as a fine white or slightly reddish, non-hygroscopic powder with a sweetish, astringent taste. It is readily soluble in cold water and in glycerin, slightly so in alcohol, and is insoluble in ether. On exposure to the air it becomes darker in color, by virtue of its reducing properties.

MODE OF EMPLOYMENT.—Alumnol is employed chiefly in solution, though also frequently as a dusting powder. As a mild astringent and antiseptic it is used in solutions of 0.5 to 5 per cent. strength. For caustic effects, a 10 or 20 per cent. solution may be employed. Where the action of several antiseptics at once is desired, alumnol may be used in combination with agents such as corrosive sublimate, resorcin, etc.; it is incompatible, however, with silver nitrate or other reducible salts, as well as with alkalies.

THERAPEUTIC USES.—The almost unirritating and non-toxic qualities of alumnol in weak solutions render it available as an astringent and antiseptic for the treatment of chronic catarrhal processes, and also in sluggish ulcerations. In acute cases, however, it generally proves too irritating to be of value. It has been employed mainly in gynecology and gen-

itourinary surgery, and, to a less extent, in general surgery, laryngology, and dermatology.

In ½ to 1 per cent. solution alumnol was found useful by Heinze and Liebreich in **gonorrheal endometritis** and in **colpitis** not of gonorrheal origin. Kontz, employing alumnol in a series of 16 gynecological cases, found that **cervical catarrh** and **simple perimetritis** yielded to its repeated use, and that **gonorrheal vaginitis** was readily cured by it. In endometritis accompanied by adnexal lesions, however, pain was augmented, owing to the irritation.

This author employed a 3 per cent. solution for lavage, a 10 per cent. solution in the treatment of **endometritis** and **erosions,** and powders and bougies of 20 per cent. strength. Marfan used 3 per cent. bougies of alumnol in **vulvovaginitis.**

Intra-uterine injections of the iodide of alumnol have been recommended by Grammatikati **as a substitute for curettement** of this organ.

Though alumnol has been claimed to exert a peculiarly destructive action on gonococci, its use as an injection in **gonorrhea** in the male has not led to results commensurate with early expectations. Casper employed it in 12 cases of acute gonorrhea, 20 chronic cases, 4 cases of gonorrheal epididymitis, 2 of post-gonorrheal adenitis, and 2 of soft chancre, administering intraurethral injections of 0.25 to 2.0 per cent. solutions; he did not find it superior to other drugs in general use. Samter confirmed these findings, though Chotzen claimed to have obtained good results. In the cases of **soft chancre** in Casper's series healing was promoted by the application of alumnol. Asch used a 10 to 20 per cent. solution for cauterizing the lacunæ and crypts at the urethral orifice.

As a surgical antiseptic, alumnol is used in 0.5 to 3 per cent. solutions. In the dressing of **wounds** and in **ulcerations,** specific or non-specific, Eraud found it to produce no irritation or pain. As a desiccant powder for wounds this author considers it efficacious.

In nose and throat practice, alumnol has been found valuable in **simple chronic** and **hypertrophic rhinitis,** in **ozena,** in **catarrhal** and **follicular tonsillitis,** and in **acute** and **chronic pharyngitis.** It is used either in a 1 per cent. solution as a douche, in a watery glycerin solution (1:5), to be applied to the affected parts, or as a powder, mixed with **starch** (10 to 20 per cent.), for insufflation. Stepanicz **found** that in acute laryngeal affections the **roughness of voice** generally disappeared after a single inhalation of a 1 per cent. solution. In chronic cases, insufflations of alumnol and starch (2 to 10 per cent.) also gave good results. Metzerott used alumnol with satisfaction not only in laryngitis, pharyngitis, tonsillitis, and peritonsillitis, but also in **edema, syphilis, and tuberculosis of the larynx.** In a case of symptomatic laryngeal edema, probably of syphilitic causation, with a severe grade of stenosis, the administration of alumnol solutions in the form of injections and the steam spray made it possible to defer tracheotomy for six months. In the case of a singer troubled with **subglottic laryngitis,** with wave-like fluttering of the vocal cords, an alumnol spray gave early relief; also in one of **chorditis nodosa** (singer's nodules), strong solutions of the remedy proved beneficial.

In otology alumnol has also been employed. In **suppurative otitis media** Heath noticed, however, that it sometimes caused persistent burning sensations, and that it tended to unite with pus in the external meatus to form stone-like pellets,—a peculiarity condemning its use in this disorder.

In dermatology alumnol has been found serviceable in powder form (12 to 25 per cent.), collodion (5 to 10 per cent.), and ointment (1, 5, and 12½ per cent.). It has proven effective in **dermatitis, acute eczema** of all sorts, and **chronic eczema,** but in syphilis and the parasitic skin affections did not yield much benefit. In **acne** and **acne rosacea** as good results have been obtained with it as by most other methods of treatment. Chotzen found alumnol efficacious in acute and chronic inflammations of the skin and mucous membranes, including **erysipelas, favus, lupus, soft chancre, and erosions.** Eraud made the statement that alumnol appeared to be useful in certain varieties of **pruritus,** especially of the anus and scrotum. S.

ALYPIN.—This is a white crystalline neutral powder, very soluble in water, which is not precipitated by alkaline fluids. Its properties are not impaired by boiling for 10 minutes. It was introduced as an anesthetic to replace cocaine. A 1 per cent. solution produced deep anesthesia of the rabbit's cornea in 50 or 60 seconds. The lethal dose in dogs and cats is about double that of cocaine. It is relatively non-toxic and is a pure local anesthetic. It has been used in a 2 per cent. watery solution. When dropped into the conjunctival sac there is a slight smarting. In about 70 seconds the conjunctiva together with the cornea is insensitive to touch. A few seconds later the ocular conjunctiva may be seized with fixation forceps without the patient experiencing pain. There is usually some dilatation of the superficial vessels, but no dilatation of the pupil. There is no interference with accommodation; it does not affect the corneal epithelium.

Alypin has been lauded by several observers, according to Wolff Freudenthal (Med. Record, July 20, 1912), but others assert that the anesthesia produced is very weak. It may be used for removal of enlarged turbinated bodies, since it does not cause, as does cocaine, a very marked contraction of the hypertrophied turbinal tissues.

Untoward Effects.—A. H. Miller (Jour. Amer. Med. Assoc., Jan. 17, 1914) reported 103 cases in which alypin had been used as a local analgesic. Of these 35 were minor surgical operations and 69 genito-urinary. In 100 of the cases analgesia was perfectly satisfactory, in 2 the analgesic caused serious difficulty and in one instance death. In the last case the patient was an apparently healthy adult, 39 years of age, who was about to undergo dilatation for stricture of the urethra. About 2 drams (8 Gm.) of a 10 per cent. solution were introduced into the urethra and bladder. Two minutes later the patient had a general convulsion, followed by a half-dozen during the next 10 minutes, with cessation of respiration and arrest of the pulse. Artificial respiration and stimulation were tried without avail. In a very similar case the patient was revived after about 2 hours' work. In a third untoward case about 1½ drams (6 Gm.) of a 10 per cent. solution was introduced into the urethra and bladder for dilatation of a stricture. In 3 minutes the patient became unconscious, and respiration became embarrassed, but the pulse remained good. Artificial respiration and inhalations of oxygen brought this patient around in about 10 minutes. The author considers Bremmermann's technique of depositing a tablet of alypin at the point of analgesic localization as far preferable to injecting an unmeasured quantity of the 10 per cent. solution into the urethra, at best a dangerous procedure.   S.

ALZHEIMER'S DISEASE.—

Two cases of this rarely encountered mental disorder, both in men of 49, were reported by C. I. Lambert (Psychiatric Bull., Oct., 1916), both with a history of alcoholism. A most profound dementia developed slowly and insidiously in both. Inattention, indifference and absentmindedness, declining efficiency, progressive impairment of memory, of retention, grasp and poverty of thought, followed by aimless, restless, foolish behavior and increasing mental dilapidation which went on apace toward an apathetic dementia, incapacity to comprehend, to talk, to walk; this was followed by a bedfast state in which the patient muttered and mumbled and fussed and fumbled, and pulled at his bedding, wet and soiled himself, chewed a little and gulped what was put in his mouth and vegetated for a time and died like a decerebrated animal. Among the more striking symptoms in these cases were the outstanding symptoms of agnosia, aphasia and apraxia.

As a rule, in such cases, there is gradual development of severe dementia with signs of cerebral organic disease. With the dementia are focal phenomena causing aprasic, aphasia and asymbolic disorders.

Alzheimer's disease is distinguishable from cerebral arteriosclerosis owing to the fact that apoplectiform attacks do not take part in the development of the high grade dementia and focal symptoms. The morbid mental phenomena develop slowly and not paroxysmally, while the signs of arteriosclerosis throughout the system are generally absent.   S.

AMAUROSIS.—DEFINITION.

—Amaurosis, formerly used to designate partial or complete blindness, has become, since the common employment of the ophthalmoscope, much more limited in its meaning and application. At present, imperfect vision not due to errors of refraction or visible pathological changes may be classified under "amblyopia"; complete blindness of one or both eyes and usually that form of blindness caused by disease of the nervous apparatus of sight, the retina, optic nerve, and cerebral centers under amaurosis.

[Both words should be so used that they refer only to certain kinds of blindness which are to be described by a preceding adjective, and unless thus defined their meaning is vague and uncertain, carrying no suggestion of etiology or pathology. When the media of the eye are transparent, normal or abnormal conditions of the fundus are as easily diagnosed by the expert ophthalmologist as are diseases of the skin by the dermatologist; therefore, except as a convenience or as a substitute for the word blindness, amaurosis might well be omitted from ocular vocabulary. Eyes blinded by disease of or traumatism to the middle or anterior third are seldom described as amaurotic eyes. H. F. HANSELL.]

Amaurosis in Brain Disease.—

Tumors or other organic changes in the brain by which the optic tract is directly compressed or the ventricular fluid is forced into the optic nerve sheaths will produce blindness. The process is a mechanical one. In the former the optic nerve fibers in the tracts are directly compressed and deprived of their function; in the latter, the optic nerve is surrounded by fluid contained within a sac of only moderate distensibility. The gradually induced compression of the nerve induces arterial anemia and venous congestion of the nerve-head and retina, which is soon followed by serous and solid exudation into the distal extremity of the nerve. Finally the optic nerve fibers become atrophied from stoppage of circulation and pressure of exudation. The loss of vision may commence in the periphery of the field and advance by slow stages toward the center until finally the entire field is wiped out; or, as may be the case in apoplexy, a section of the field, one-half, one-quarter, or less, or the region about the fixation point and including it, is suddenly lost. Continuation or extension of the brain lesion will be followed by loss of the entire visual field.

Amaurosis in Nephritis.—

Disturbance of vision may be caused by hemorrhage or edema into the cerebral centers, by pressure upon the chiasm or tracts, or by the action of the poison of uremia, by which the brain functions are held in abeyance. In the first and second it may affect one or both eyes and be partial or complete. In the third it comes on rapidly, involves both eyes, and disappears in a few hours or in a day or two. There are no ophthalmoscopic changes visible in the retinal circulation or structural alterations in the nerve or retina. The blindness is strictly cerebral. In the early stages of hemorrhage or edema the eyegrounds are normal; later they show the signs of intracranial pressure. In a man who died twelve hours after cerebral hemorrhage and who was unconscious from the time of the attack until his death, the ophthalmoscope showed only moderate dilatation and tortuosity of the veins. These forms of amaurosis are not to be

confounded with the amblyopia of albuminuric retinitis, in which the vision is affected in several ways; by edema of the nerve-head, edema of the retina, hemorrhage in the foveal region, and patches of degeneration of that area. The diagnosis may be established by the ophthalmoscope.

> The writer describes 3 patients who were blind for longer or shorter periods after blows on the back of the head that did not fracture the skull. He ascribes the blindness to a traumatic affection of the occipital lobes, shock or hemorrhage, or both. L. Newmark (Jour. of Ophthal. and Otolaryn., May, 1914).

> Case in which the blindness came on gradually first in one eye and after some time in the other. There had been lancinating pains and some tendency to ataxia for a few months. The patient was a man of 49, and there was no history of headache or ocular paralysis. A number of cases on record teach the necessity for curing the syphilis in the secondary stage at least as the only means to certainly ward off atrophy. L. D. Espejo (Cronica Medica, Nov., 1917).

Amaurosis in Hysteria.—Neuroses, the result of an unknown derangement of the nervous system originating within the body or of traumatism, may reduce or altogether destroy temporarily the visual power in one or both eyes, rarely the latter. The traumatism may be ocular or involve any other part of the body. In order to induce blindness or even amblyopia the causative disease or injury must affect an individual of peculiar or susceptible organization and makes manifest a tendency toward magnification of trifles for the sake of bringing into prominence the ego or for the sake of imposition. In traumatic cases the diagnosis between hysterical amaurosis and malingering is not always easy. Both offer no evidence externally or internally in the eye of any mark of injury or disease sufficient to account for the symptoms. In hysteria the well-known stigmata may be found—tubular field, transient and recurring ocular paralyses, reversal of the color field, well-defined patches of localized anesthesia of the skin, inexplicable and transient pains distributed anywhere and everywhere in the body and created by cleverly directed interrogation. The majority of the subjects are women who are more or less mentally unbalanced by disease of the sexual organs or by physical or mental idleness. The malingerer is usually a man who resorts to the excuse of blindness in order to avoid unpleasant or dangerous duty or to collect damages from a rich corporation. The symptoms of hysterical amaurosis are altogether subjective and of cerebral origin. The eyes cannot be held responsible.

Amaurosis in Spinal Disease.—Primary atrophy of the optic nerves preceding or accompanying disease of the spinal cord and spinal nerves is a common affection. It is "primary" because it is initiated and carried to its finish without inflammation of the optic nerve visible to the ophthalmoscope. There is no edema or exudation. The disk margins remain clear cut and well defined. The first noticeable change is a loss of the normal pink color on the temporal half of the papilla and a diminution of the size of both the arteries and veins of the retina. Gradually the vascularity becomes less, the nerve becomes paler and finally white, all the fine vessels having become absorbed from the surface. Contemporaneously with the

atrophic process the vision declines until complete amaurosis results. Early in the disease the field for colors is concentrically contracted or the perception of green is lost, and the retina becomes less sensitive to light or the optic nerve less capable of transmitting feeble stimulation. The affection is binocular, although one eye is usually more affected. Secondary atrophy, that following inflammation of the intraocular end of the optic nerve, presents entirely different ophthalmoscopic appearances, and no confusion need arise in the diagnosis between the two affections. The diseases of which primary optic nerve atrophy is a prominent symptom are tabes, disseminated and lateral sclerosis, dementia paralytica, and paralysis agitans. The pupillary and visual disturbances may precede by many years the development of spinal affections, particularly posterior sclerosis, and many of the so-called idiopathic cases really belong to this class. The writer believes this is true also of paralysis agitans. He has at present a patient who seven years ago had incipient atrophy of the optic nerves with shallow excavation and for the past two years has slowly advancing paralysis agitans.

Amaurosis following Hemorrhage. —After extensive loss of blood from any cause, but especially from disease of the stomach, intestines, or uterus, blindness affecting both eyes, commencing two or three days after the hemorrhage and advancing rapidly, may ensue. The ophthalmoscope shows marked ischemia of the retina with low-grade edema of the nerve-head. The blindness may be complete and permanent, terminating in optic nerve atrophy; or, in an individual with good recuperative power or when the loss of blood has been moderate, restoration of sight may be complete.

Amaurosis in Pregnancy.—Toward the completion of the term of pregnancy or during confinement, vision may be entirely suspended in both eyes for some hours or days. The amaurosis is usually associated with convulsions or other signs of puerpural septicemia. It should be regarded as a strong indication of intense and general poisoning. The fundus either shows no deviation from the normal or the retinal veins are distended and dark in color, the nerve-head is slightly edematous, and an occasional hemorrhage is found in the retina. After safe delivery, vision rapidly returns and the eyes are restored to their previous condition. Atrophy of the nerve and permanent amaurosis as a result of pregnancy alone have not, as far as the writer knows, been described, yet he has seen cases in which no other cause for the blindness could be assigned.

Case of amaurosis gradually developing in the course of pregnancy. The first signs of optic neuritis were noted about the fourth month; both eyes were affected and external causes could be excluded. The optic nerve was atrophied when the patient was first seen and the indications for interruption of the pregnancy were beyond question. Sight began to improve at once, and within two weeks vision was restored in the right eye. The other eye was first involved, and the nerve was atrophic beyond relief. The woman was a multipara of 37, with 8 children, and the author deemed it necessary to insure future sterility by an operation on the tubes. The case confirms anew the importance of immediate interruption of the pregnancy in case of optic neuritis from this cause. Holzbach (Zentralbl. f. Gynäk., May 23, 1908).

A form of amaurosis or amblyopia, not accompanied by ophthalmoscopic signs, or, at least, by none adequate to account for the condition, may supervene during pregnancy, parturition, or the puerperium. Rarely it may assume the form of a hemianopic defect or of a central scotoma in the fields of vision, and still more rarely of hemeralopia (night blindness). It is often associated with such signs and symptoms of toxemia as headache, edema, eclampsia, and scanty urine containing albumin, casts, and blood. Recovery occurs, as a rule, within a few hours or days. Stephenson (Ophthalmoscope, March, 1910).

Amaurosis from Fracture of the Skull.—Numerous cases have been recorded of complete blindness of both eyes some months after a traumatism of the skull. The common lesion is fracture at the apices of the orbits with or without involvement of other bones at the base. Hemorrhage from rupture of a large blood-vessel either anteriorly at the base or involving the basal or cortical centers of vision, a frequent complication of fracture of the skull, will destroy vision.

In the latter lesion the amaurosis is more rapid in its onset and temporary. Absorption of the blood is followed by gradual return of vision unless the nerve structures have been destroyed by the insult or by pressure.

Description of an epidemic of transient blindness. Of 5 persons on board a small vessel soon after its arrival, 3 were taken suddenly sick and complained of loss of vision, but there was no fever; 2 died within 3 days, a man and a woman. The man who recovered became blind the fourth day. After 12 days of amaurosis, vision gradually returned, although there were still evidences of optic neuritis. Three other cases of this apyretic amaurosis developed in the same locality, without contact with the first group. One of the men was just recovering from influenza. No causes of common intoxication could be discovered in the first group. Verger and Moulinier (Jour. de Méd. de Bordeaux, Feb. 15, 1919).

The writer urges that not a minute be lost before training those suddenly blinded. Such a person is like a babe just born into a new world. From the very first, while still in the eye hospital, his training in writing with a guide frame and in reading the Braille type should begin, without waiting to ascertain whether vision is entirely lost or not. All the men could read and even write the Braille fluently by the time they left his service and had been initiated into manual labor, such as weaving rugs, making brooms and brushes, resoling shoes, or doing light garden work. Ginestous (Prog. Méd., June 8, 1919).

Congenital and Hereditary Amaurosis.—Infants born with ocular or cerebral defects, such as buphthalmus, microphthalmus, or other deformities, or "amaurotic family idiocy," by which the essential parts of the eye or brain are wanting or so disturbed that function is absent, are hopelessly blind. Hereditary optic nerve atrophy, transmitted usually to males through the female line, appears suddenly between the twentieth and thirty-fifth year as a loss of central vision. The scotoma increases and the periphery of the field becomes contracted until the patient is permanently and totally amaurotic.

Having found in the family history of an inmate of the Missouri School for the Blind the presence of cataract in all the members of the family for at least five generations, the writer after receiving the opinions of 152 oculists concludes as follows: 1. All whose life work brings them into relationship with the blind should be aware of the dan-

gers connected with the marriage of a blind person. 2. The blind themselves should be warned of the danger to their children in case of marriage. 3. A distinction must be made between hereditary and non-hereditary forms of blindness. 4. Legal assistance should be invoked to prevent blind people from marrying. 5. This law should apply only to those cases of blindness in which heredity has been proved. With the exception of glaucoma and cataract, these diseases usually manifest themselves at or before the marrying age. 6. A law compelling every person to have an oculist's certificate before marriage, though idealistic, would be impracticable. 7. The general public should be educated in the dangers arising from hereditary blindness. C. Loeb (Annals of Ophthal., Jan., 1909).

The causes of blindness in a series of 1100 children are classified by N. B. Harman (Brit. Med. Jour., Aug. 29, 1914) into 3 groups: Injury or destruction of the cornea through surface inflammation within the eyeball or optic nerve; congenital defects of the eyes. Surface inflammation involved the eyes of 351 children, and of this number no less than 266 had ophthalmia neonatorum, giving a proportion for this disease of 24 per cent. of the total cases of blindness. Only 47 cases were due to purulent conjunctivitis of later years, and 38 to phlyctenular keratitis. Syphilis was the cause of 190 cases of interstitial keratitis, of 126 cases of disseminated choroiditis or other blinding lesion of the posterior half of the eyeball, and of 16 cases of congenital blindness. Syphilis, therefore, accounted for a total of 343 cases of blindness, or 31.7 per cent. of the whole 1100 cases, or of considerably more than were due to gonorrheal infection. This is in part the result of the recent more or less general use of some prophylactic agent in the eyes of the newborn to prevent gonococcic infection. Since 1904 the figures show that there has been a definite reduction in the proportion of cases of blindness due to the gonococcus, while the proportion due to syphilis has risen.

In a study of the causes of blindness, H. L. Gowens (Hahn. Mthly, Apr., 1914) shows that 88.58 per cent. of all blindness is preventable as against 11.42 per cent. incurable and non-preventable blindness. Even after eliminating purulent ophthalmia and high myopia there still remains 85 per cent. as a percentage of blindness which is conceded to be preventable blindness as against 15 as a percentage which is non-preventable and incurable.

H. H. Stark (Jour. Amer. Med. Assoc., Oct. 30, 1915), in reporting cases of eye complications of sinus disease, reviews the literature. Of 88 cases reported, the optic nerve was involved in 52. Variations in the pupil occurred as one of the earliest symptoms. Exophthalmos occurred in 11, and involvement of the extrinsic muscles in 11. Central scotoma was the most definite, and the one on which the author most relies.

W. H. Bates (N. Y. Med. Jour., Feb. 3, 1917) cites a case in which he employed a new method of treatment for a developing glaucoma, and a previous gradual loss of sight for 25 years. The patient, a woman, had received treatment from many physicians for her eye conditions during this time. Bates treated her for the following conditions: Incipient cataract, vitreous, cloudy with floating bodies; neuritis, with partial atrophy of the optic nerves; retinitis, with obliteration of many blood-vessels; choroiditis disseminata; glaucoma of the left eye; connective tissue in the anterior chamber of the left eye, obscuring the iris and pupil; functional myopia; functional divergent and vertical squint. An acute glaucoma developed and was treated at first by drugs. With the assistance of Dr. C. Barnert an iridectomy was performed, and while pain and tension were relieved, the vision was not improved. Mild, recurrent attacks of glaucoma occurred. Bates then employed the **central fixation method** of treatment, and obtained such excellent results that the patient at the end of a comparatively short time was able to travel on the subway, attend social functions, and could see clearly the lights across the Hudson River. In 6 days the sight of the right eye had improved to more than $\frac{1}{10}$ of the normal. The method demands the use of

the memory and the imagination. A small black spot on the Snellen card was imagined, and at the beginning of the treatment, the period imagined was imperfect. The patient had to imagine this spot as perfectly black and stationary at all times; then to be conscious of seeing a part or all of a letter without losing the period. Central fixation meant to her a passive or relaxed condition of the eyes and brain. The objective symptoms all disappeared instantaneously when the patient was conscious of central fixation, and the organic lesions were gradually seen to improve. With the blood-vessels the changes were more slow; but with the cloudiness of the lens, central fixation was followed immediately by an increased transparency.

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AMBLYOPIA. — DEFINITION.

—The word "amblyopia" signifies, without specializing the cause, that the acuity of vision is below the normal. The degree of the loss of vision is not suggested by the word itself, nor has there been any attempt, as far as I am aware, to define its limitations. It has been inherited from the preophthalmoscopic times, when the two words amblyopia and amaurosis were commonly used, the former to mean dull vision and the latter, blindness.

[Today we seldom hear of amaurosis, but we have tenaciously held to amblyopia. Its use is convenient, but unless preceded by a descriptive adjective, such as toxic, hysterical, its meaning is indefinite and vague. The sense in which the word is properly used is the express partial loss of vision due neither to dioptric abnormalities nor to visible organic lesions, or, as expressed by the older writers, "amblyopia without ophthalmoscopic appearances." It is, therefore, not a disease, but a symptom, and is due to many different and varied causes. H. F. Hansell.]

The varieties of amblyopia are usually classified into organic from toxic and intracranial causes, functional exanopsia (disuse, non-use, argamblyopia); hysterical, simulated, and from exhaustion.

Toxic Amblyopia.—The ingestion of or absorption into the system through the lungs, intestinal tract, or skin, of large quantities of certain substances without adequate elimination, or of small quantities in the case of some susceptible organisms, will produce a loss of vision varying in degree from slight up to total blindness. The commonest agents are alcohol and tobacco in combination, lead, quinine, methyl alcohol, Jamaica ginger, coffee, mercury, phosphorus, chloral, opium, ergot, the salicylates, ptomaines. The sight is affected by these substances in several ways—by altering the constituency of the blood and lessening its nutritive value to the ocular structures; by exciting disease of the retinal nerve-cells leading to degeneration of the cells and of the optic-nerve fibers connecting them with the brain-centers and inducing structural changes in the centers for vision. The amblyopia may be acute, as in quinine and methyl alcohol, or chronic, as in tobacco and alcohol poisoning.

The symptoms common to the chronic form are:—

Loss of Vision.—The deterioration is gradual and is usually neglected by the patient until the ability to read is diminished or abolished. Examination shows that vision has fallen to one-half or more for distance and near and is not to be improved by glasses. The patient complains of a bluish-gray smoke or mist constantly before the eyes, and of partial night-blindness. He has no pain and rarely phosphenes or

other signs of irritation of the retina or nerve.

Central scotoma, either relative (colors only) or absolute. Early in the affection, probably contemporaneous with the beginning of the deterioration of vision, the perception for green in the small region of the field controlled by the fovea centralis is lost. Then follows the perception for red and possibly blue. The scotoma may be confined to these colors. Should the disease advance, the scotoma becomes absolute, the perception of all objects being lost in an area of about 10° from the fixation point. The periphery of the field retains its normal dimensions until the onset of optic nerve atrophy, when it undergoes a concentric narrowing.

Papilla Changes.—The ophthalmoscope shows in nearly all instances a whitening of the temporal half of the papilla, with retention of the normal coloring and vascularity of the nasal half. The retina and choroid are unchanged. Even the macula, the point of the fundus which is symptomatically most involved, appears healthy. In about one-third of the cases the optic disk is slightly hyperemic early in the disease and the vessels on the disk are veiled, reflecting the earliest signs of optic neuritis.

Acute poisoning from absorption of methyl alcohol, quinine, pure spirits, etc., causes sudden and complete blindness, even to the loss of perception of light. The action of the poison may be sudden or cumulative. A man of 35 was exposed by the nature of his occupation to the fumes of varnish. He absorbed them through the lungs and the skin of the hands and arms. Feeling in his usual good health when he went to bed, he was awakened several hours later by some cause unconnected with his eyes and discovered he was totally blind. Examination of his eyes the following day disclosed excessive anemia of the disks. The arteries and veins of the retina were invisible a short distance from the nerve-head. A boy of 19 drank an unknown quantity of "white whisky" (95 per cent. alcohol). He was blind the next morning and, except for the temporary return of perception of light lasting a few days, remained blind. The ophthalmoscopic appearances were similar to those in the former case. The prominent symptoms of acute toxic amblyopia are illustrated by both cases: Sudden and complete blindness, partial temporary recovery, ischemia followed by atrophy of the optic nerves and retinas, and permanent blindness.

Amblyopia from Intracranial Causes.—In the preceding paragraph the morbid processes are presumed to be limited to the nervous mechanism of the eye, lying anterior to the chiasm or, if they invade the cerebral tissues, the involvement is secondary and may be considered as a complication. In the intracranial amblyopias the original lesion is cerebral, the secondary in the optic nerves and retina. Uremia of Bright's disease, of pregnancy, and of scarlet fever is a common cause. The amblyopia is usually binocular, rapid in its course, and leads often to complete, but temporary blindness. The prognosis is good. No changes in the eye-grounds commensurate with the degree of loss of vision are to be seen. The retinal veins are distended, dark, and tortuous, and the edges of the disk veiled by edema of the nerve and adjacent retina. The cerebral vessels present a similar condition, namely, reduced supply of

arterial blood, venous stagnation, and diffused serous exudation into the brain substance. The foreign elements contained in the blood doubtless are a contributing cause to the disturbed brain functions. With the establishment of free secretion of urine or artificially induced active diaphoresis the poison is eliminated from the blood, the serum absorbed, and the vision and cerebration restored; or, the kidneys refuse to act, the skin cannot be stimulated, and death ensues.

Rarer forms of amblyopia due to obscure intracranial lesions are the "crossed" and the "hemianopsias." Mills says (Posey and Spiller): "As the fibers of the macular bundles are undoubtedly distributed to the pregeniculatum, complete destruction of this body, or of a special portion of it, would cause central amblyopia of the crossed variety." In the hemianopic variety one-half of the macular field is lost and the other half preserved. Thus one-half of a word or other small object close to the eyes is obscured and can be seen only by movement of the ball. In explanation Mills further says: "A strictly limited lesion of the calcarine cortex on the one hand and of the angular region on the other may cause blindness in half of the macular field of the corresponding sides."

Hysterical Amblyopia.—The features characteristic of this affection are partial or complete blindness, monocular or binocular, without discoverable changes in the ocular structures or signs in the eye or elsewhere in the body of organic disease of the brain or nervous system. The loss of vision may arise spontaneously, or appear at the termination of an attack of general hysteria, or be due to a slight trauma-

tism to the eye or head. The traumatism is, as a rule, slight and out of all proportion to the seriousness of the subsequent complaints. Amblyopia may be the only ocular symptom or it may be complicated by ptosis, recession of the near-point, pupillary inequalities, or disturbances in the field of vision. The alteration in the size and form of the field presents three possible features: concentric contraction, which is not in the least characteristic of hysteria; reversal of the normal limits of the color fields, and the tubular field. Traumatic cases recover promptly and wholly after the cause, for instance a suit for damages, is removed. Cases of spontaneous origin and those dependent upon functional derangements of the nervous system are more persistent, often recur, continue weeks and months, and recover only upon the restoration to health of the individual. It must not be forgotten that blindness without ophthalmoscopic findings or evidence of disease of the cerebrospinal system may not always be diagnosed as hysterical, and that it may have an organic cause to become manifest in time. To make the diagnosis positive it should be associated with at least some of the well-known stigmata of hysteria.

Simulated Amblyopia.—The differential diagnosis between simulated and hysterical amblyopia is rendered difficult by the similarity of the two affections and because both occur in the same class of patients, the neurotic and those of hypersensitive organizations. Pretended, feigned, or simulated blindness is found among recruits for the army and navy services, those who wish to escape positions in which danger or punishment may be incurred, and those who wish to create false impressions and exaggerated estimates of their

physical disabilities, especially in lawsuits for damages. Simulated amblyopia of both eyes is rare and detection difficult. Reliance must be placed on the action of the pupils and the want of relation between the apparently normal eyes and the symptoms. The monocular form, however, may be, as a rule, easily detected. The ophthalmoscope shows clear media and healthy eye-grounds; a strong spherical lens placed before the sound eye will prevent accurate vision in that eye beyond the focal distance of the glass; a prism of 5°, base down or up, will give vertical diplopia; a prism of 10°, base out, will cause a manifest rotation of the eye inward, unconsciously made to fuse the horizontally induced double images; a lead pencil placed before the sound eye will not interrupt reading; the pupils respond to light and convergence almost uniformly. The tests will more successfully deceive the patient into admitting visual power in the assumed blind eye if his attention is directed by them to the sound eye. Radiography is also valuable in the diagnosis. An individual may claim that the blind eye contains a fragment of glass or other foreign material impervious to the rays. In such cases a shadow is cast on the plate when the claim is true. In trolley accidents it frequently happens that the glass of the doors or windows is shattered and the hysterical or fraudulently inclined passenger asserts that he was blinded by the entry and retention in his eye of glass. Examination with the ophthalmoscope cannot invariably exclude the presence of the foreign body, particularly when it has lodged in the ciliary region or when the media are clouded.

Amblyopia Exanopsia.—*From congenital defects* in the ocular structures,

such as cataract, polar and lamellar; coloboma of the lens or uveal tract; persistent pupillary membrane; albinism. Rays of light are obstructed in their passage through the eye by the opaque media, they are not clearly focused on the retina by reason of irregular refraction, or they fall upon insensitive retinas or those unsupported by choroidal pigment. In these cases it is probable that early in life the retinal centers in the brain are active and do not, either by disease or congenital anomaly, contribute to the blindness. The cataracts may be removed and vision restored when the operations are performed at an early age. Later, when the brain-centers have been trained and the habits of special sense perception have been formed, operations, although surgically successful, do not materially improve vision.

From Defects of Refraction.—In grades of hyperopia from 2 D. to 5 D. in childhood, binocular vision may early become unattainable. The child unconsciously, in order to obtain good vision, makes extraordinary claims on the accommodation. But the ciliary muscle (accommodation) is supplied by nerve power by the third or motor oculi nerve, which also supplies the muscles of convergence. Therefore, excessive stimulation of accommodation or that surpassing the normal relation between accommodation and convergence compels a proportionately equal degree of convergence. Since both eyes cannot converge simultaneously in distant vision, one eye assumes the abnormal convergence and the other eye is used for fixation. Both eyes retain their normal power of rotation, but each becomes in a sense independent of the other: the one is used for seeing; the other squints. The

former has been the better eye from the beginning, either by reason of less error of refraction or more perceptive retina. The latter gradually becomes amblyopic from disuse. The retina loses its sensibility, the optic nerve its conductility, and the cerebral centers their function. In some children no reason can be assigned for preference of one eye. The error of refraction may be no greater and the rotatory power no less in the squinting than in the fixing eye. Here we must assume that the fault lies in the retina, nerve, or brain. Improvement of vision may be obtained by the forced use of the eye and the compulsory activity of the cerebral center, but vision equal to that of the non-squinting eye is seldom or never acquired unless the usefulness of that eye is destroyed by accident or disease. Habit and the cultivation of the visual apparatus that accrues from habit can not be ignored. Should, however, the treatment for defective vision be instituted very early, before anesthesia of the nervous apparatus of the squinting eye has developed, an appreciable benefit may be gained by the use of the amblyoscope, closure of the fixing eye by bandage, or atropinization of that eye.

Amblyopia from Exhaustion.—Amblyopia in consequence of excessive indulgence in coitus or masturbation has been recorded. It is a purely nervous affection. Upon removal of the cause and the administration of strychnine the cure is generally rapid and complete. Sudden loss of blood in large quantities, occurring sometimes in intestinal ulceration, after delivery of the child in confinement, rupture of blood-vessels by ulceration or accident, may be followed in a few hours by temporary loss of vision. The ambly-

opia becomes permanent only in cases of degeneration of the ganglion cells of the retina or of the fibers of the optic nerve.

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AMENORRHEA. — DEFINITION.—Absence of the menstrual flow in women of a suitable age who are not pregnant. Suppression of menses, the menstruation having ceased through some local or remote disorder, is also termed amenorrhea.

VARIETIES. — Amenorrhea may be *complete,* when the menstruations will have completely ceased; *comparative,* when it appears occasionally; *primary,* when the menstruation has not presented itself at the age of puberty nor subsequently; *secondary,* when transitory or accidental, or, having already appeared, the menstruation ceases.

SYMPTOMS.—No other symptom than absence of the menstruation may be present, or the monthly flow may be absent and the general attendant phenomena usually preceding menstruation occur. Frequently the patient complains of headache, heat-flashes, fever, nausea and vomiting, and heaviness in the abdomen. Concomitant nervous disorders may form the basis of acute manifestations, hysterical especially. When the amenorrhea is due to obstruction, whether congenital or acquired, the patient does not experience severe pain, but rather a continuous dull aching in the pelvis and over the sacrum, aggravated at the periods when the menstruation should occur by the symptoms above mentioned, known as menstrual molimina.

Pure suppression of the menstruation rarely causes symptoms, espe-

cially when the impending general disorder is the cause of the amenorrhea.

The menstrual flow may be substituted by a profuse leucorrhea which is thick, viscid, and of a yellow or greenish-yellow color. Remote symptoms may present themselves, doubtless of reflex origin.

ETIOLOGY.—The discussion of the causes of amenorrhea is rendered difficult by our want of knowledge of the forces which produce the periodical recurrence of menstruation. Primary amenorrhea is generally due to imperfect or insufficient development. In cold countries the individual matures more gradually and the menstrual flow appears later than in warm countries, where development is rapid, but where, also, women enter stages of decrepitude at an earlier date. Anatomical imperfections and anomalies, the absence of any of the genital organs, or a rudimentary or infantile uterus may thus account for the total absence of menstruation. Imperforate hymen is a frequent, though easily recognized, cause of amenorrhea.

Whether we ascribe the periodical occurrence of menstruation to nervous irritation, to the influence on the mucous membrane of the uterus of a superabundance of lime salts in the blood or to the chemical influence through the blood of a secretion of the corpus luteum, the causes of amenorrhea can be divided into four classes:—

> Many cases of amenorrhea are traceable directly to absence of corpus luteum owing to the degeneration of unruptured follicles. This probably accounts for the good results obtained in some cases from corpus luteum organotherapy. Emil

Novak (N. Y. Med. Jour., June 17, 1916).

> An increase in amenorrhea has been observed since the beginning of the war, in young girls who have reached puberty. Amenorrhea is not infrequent in cases where the conditions of life are changed at the time of puberty. In the present instance the change is one of diet. This differs from the pre-war diet in poverty of flesh and fat. There is also a prolonged physical and intellectual weakening. M. Graefe (Münch. med. Woch., lxiv, No. 18, 1917).

Nervous Disorders.—Grief, anxiety, fright, and anger are as many possible primary causes, especially if the patients are poorly fed. According to Bloom, probably not less than 33 per cent. of women emigrants under 30 years of age suffer from suppressed menstruation after a sea-voyage. Many have abdominal distention, and not infrequently girls have been innocently charged with being pregnant. Obstinate constipation is a common symptom. The true etiology is largely psychical and neurotic.

> The causes of primary amenorrhea at puberty not due to congenital atresia may be distinguished into three varieties, viz.: 1. Cases without discoverable cause, in which the genital organs are apparently perfectly normal. 2. Those due to some congenital defect. 3. Amenorrhea accompanying some general disease, as diabetes or tuberculosis. In the first, local or general treatment may cause appearance of the menses, the prognosis in the other two varieties being unfavorable. The writer cites a case in which menstruation occurred after grafting of a healthy ovary from another subject in the uterine wall. V. le Larier (Paris Thesis; Zentralbl. f. Gynäk., Nu. 35, 1905).

Women who either greatly fear or greatly desire to become pregnant, newly married women, and women

who are confined in prisons or insane-asylums furnish a large proportion of the cases. Removal from country to city or *vice versâ*, especially when coupled with nostalgia, is a prolific cause. On general principles, change in the mode of living or of climate, especially with an intervening sea-voyage, appears to frequently act as the etiological factor.

Amenorrhea may be an early symptom of brain tumor and in acromegaly may precede every other symptom by several months and be followed by optic atrophy.

General Affections.—Amenorrhea frequently occurs after a serious illness, such as typhoid fever, eruptive fevers, mumps, pneumonia, or during the course of any chronic disease, diabetes, cancer, malaria, at the onset of severe syphilis. Intoxication of the system, as in morphinism, alcoholism, and hydrargyrism, is also a recognized cause. Syphilis is also thought capable of causing amenorrhea.

Lutaud, of Paris, reported 18 cases in which the morphine habit caused amenorrhea. It is usually complete and accompanied by loss of sexual desire, but the functions are re-established if the habit be broken.

> Three cases, aged from 28 to 42, in which amenorrhea persisting from six to eight years was probably due to syphilis. They all exhibited characteristic symptoms of tertiary syphilis, and were subjected to a rigid mercury and iodide treatment which resulted in the return of the menstrual flow. Meirowsky and Frankenstein (Deut. med. Woch., Aug. 4, 1910).

> The writer observed a case in which the amenorrhea was due to an X-ray examination. The patient, a girl of 14, robust and of a good family, had swallowed a needle, and was examined for ½ hour with the X-rays, which entailed a severe dermatitis. Although she had been menstruating for nearly 2 years, she ceased to do so after the X-ray exposure. After 3 months she began to have severe headaches and at times abdominal pain, especially in the left flank. Ovarian treatment, mustard foot baths and purgatives, applied at the approximate menstrual dates failed to bring any result. Siquot (Rev. Med. del Rosario, Aug., 1918).

It may be consequent upon an acute or chronic surgical affection, a blow, or injury. Luxurious living and want of exercise, obesity, and excessive intellectual labor at the period of puberty, when not counterbalanced by fresh air and active exercise, may retard the development of the generative organs and thus induce the disorder.

Blood Disorders and Wasting Diseases.—Anemia and idiopathic chlorosis, pernicious anemia, leukemia, and Hodgkin's disease are the most prominent factors. The following causes of waste—and directly, therefore, of amenorrhea—are also to be remembered: Hemorrhage, albuminous discharges; hemorrhage from piles, scurvy, purpura, and injury, as in hemophilia; hemorrhage from the stomach, as in gastric ulcer; from the lungs, or from the nose, and from a rare disease produced by a parasite in the duodenum: the *Ankylostoma duodenale*. Long-continued suppuration, albuminuria, chronic diarrhea, malignant ulcers, tubercular disease, all impoverish the blood, and so may cause anemia. All diseases that cause wasting of the body finally cause the menstruation to cease. Chief among these are phthisis, diabetes, caries of bone, protracted or

febrile illness; anorexia nervosa, the patient wasting because she will not eat; and gastric ulcer.

The occurrence of menstruation is associated with increased vascular tension; hence, any condition which decreases tension will favor amenorrhea.

Lesion of Genitourinary Organs. —Amenorrhea may be associated with any lesion of the genital tract, though less likely to occur in inflammatory conditions. Adhesions from pelvic peritonitis are an occasional cause of hyperinvolutions of the uterus and amenorrhea as a symptom.

Atrophy of the ovaries, senile atrophy following pregnancy, and cystic ovarian degeneration are among the less common etiological factors. A most complete examination of the pelvic organs, under ether, if necessary, should be made in such cases.

Exposure to cold during menstruation, by inducing congestion of the pelvic organs, is one of the most active exciting causes, especially when supplemented by a local chronic disorder. The most important condition with which this disorder might be confounded is pregnancy.

PATHOLOGY.—A pathological identity can hardly be attributed to amenorrhea, owing to its complex causes, the diverse physiological conditions peculiar to the cases, and the diathetic conditions that may be present. The fact that the true nature of menstruation itself is unknown adds another objection, and it may safely be said that the pathology of amenorrhea is that of the diseases causing it, until the local disorders brought about by each will have been determined.

DIAGNOSIS.—Primary amenorrhea—that is, total absence of menstruation—is usually due, as already stated, to the absence of one or more of the organs of generation. It must be distinguished from retention of the menses due to atresia of the cervical canal, of the vagina, or of the vulva. In the latter case no menstruation has existed, but the general premonitory symptoms of menstruation have occurred, though followed by no menstrual flow. Cases in which one or more of the organs are absent are not very infrequent, while cases of imperforate hymen are comparatively common.

PROGNOSIS.—Amenorrhea due to absence of any of the organs is, of course, incurable. The same may be said where the approach of the menopause or other conditions point to premature senility of the uterus, which involves the inhibition of the menstrual period. Although amenorrhea, when due to a serious chronic disease, is usually cured with difficulty, hope may always be entertained when the causative disorder is not in itself a fatal one. Return of the menstruation in any chronic disorder, when the blood presents its normal appearance, is an encouraging sign.

TREATMENT.—No woman should be treated for amenorrhea until the possibility of its being caused by pregnancy has been eliminated, if necessary by a careful physical examination. Not infrequently will pregnant women desirous of escaping the responsibilities of maternity seek a consultation with the hope that some drug shall be administered or instrument inserted which will terminate the condition.

Amenorrhea should always arouse concern; it may be the first symptom of acromegaly, to which it stands in

about the same relation as ordinary goiter does to exophthalmic goiter, the hypophysis cerebri being so often involved. The amenorrheic should take special pains to avoid chilling, especially of the feet, and every catarrhal affection should be treated with great care. Three such patients in the writer's practice had previous sinusitis, commencing in 1 case at the time the menses became irregular. Special care should also be paid to treatment of syphilis in this connection. Rosenberger (Zentralbl. f. innere Med., Feb. 25, 1911).

Curetting was found to aid in the restoration of menstruation in a large number of 111 cases of amenorrhea. The uterine mucosa undergoes cyclic changes even without the menstrual hemorrhage. The scraps obtained by curetting show whether the mucosa is comparatively normal or atrophied. By this means the writers discovered in 5 cases in the uterine mucous membrane a tuberculous process which had never caused symptoms. Novak and Graff (Zeit. f. Geburtsh. u. Gynäk., Apr. 5, 1921).

It should be kept in mind that amenorrhea is a symptom, and its cause be diligently sought as a preliminary measure to treatment. Drugs which are considered to exert an influence in promoting the menstrual flow are known as emmenagogues, and are divided into two classes, medicinal and physiological.

Severe physical shock or fright sometimes causes the menstruation to return suddenly.

When the arrest of menstruation is due to exposure to cold, **warm baths** and **vaginal injections, sinapisms** to the thighs and calves of the legs, **saline laxative** and **manganese-binoxide** pills (2 grains each), 1 or 2 after each meal, are frequently successful. This drug acts by increasing the vascularity of the pelvic organs.

The **permanganate of potassium,** or the **lactate,** in 1-grain doses three or four times daily, after meals, act in the same manner.

Potassium permanganate may be given daily until the catamenia appear and complete their course, when the salt should be discontinued; it should be recommended four days before the access of the next period, and continued until the flow ceases. It is useful in girls who, on leaving the country and coming to town, suffer from arrested menstruation; also in the amenorrhea induced by sea-sickness and in the case of women, between 30 and 40, generally married, who while rapidly increasing in weight suffer from a diminished menstruation. Potassium permanganate is given up to 1, 2, or more grains in pill form thrice daily, after meals. The pills should be made after the following formula: **Potassium permanganate,** gr. j; **kaolin and petroleum cerate,** in equal parts, q. s. Certain observers deny that the permanganate produces abortion, but some cases of abortion apparently due to the drug have been observed. (Practitioner, Feb., 1911).

In the amenorrhea following sea-voyages the preparations of **manganese** and **oxalic acid** hold the first place.

When the manganese preparations fail, **santonin,** 10-grain doses at bedtime, is especially valuable in chlorotic subjects.

The general system should be invigorated by attention to diet, sleep, and clothing. **Out-of-door life, light exercise,** and **sunlight** are most important. This is especially the case when there is rapidly increasing obesity. In the latter case the **diet** should be regulated, **saline laxatives** administered, or a cure at **Marienbad** recommended. The administration of **thyroid extract** is especially effective in premature menopause from obesity,

and should be associated with **active exercise.** Stimulation of the ovaries and uterus by the **faradic current** is especially efficient in such cases.

Cupping or **scarifying the cervix** is sometimes successful. These means increase the pelvic congestion and tend to counteract uterine or ovarian torpidity.

Rudimentary organs or atrophy of the uterus, if not too great, should be treated by **dilatation of the uterus** with tents and stimulated by the **faradic current.** The introduction of a **stem pessary** which is to be worn for a number of months not infrequently increases the growth of a rudimentary organ and establishes the function of menstruation. **Exercise** and **nourishing food** should also be given. **Sea-bathing** is of assistance in such cases.

> In amenorrhea due to infantile uterus the writer recommends hygienic and tonic measures; the **uterus slowly dilated** with graduated dilators; **iodine** or 95 per cent. **phenol** applied to the endometrium; and later the insertion of a **stem pessary** and the careful administration of **thyroid extract** or **corpus luteum,** given continuously over a considerable period of time. Loop (N. Y. State Med. Jour., Apr., 1917).

The rheumatic diathesis occasionally plays a part as an etiological factor. In such cases the **ammoniated tincture of guaiac,** 1 dram in milk three times a day, or the **tincture of colchicum root,** 10 drops every three hours until the bowels become free, will sometimes restore arrested menstruation. The **salicylate of sodium** is also valuable in this connection. **Apiol,** 4 grains daily in 1-grain pills, for fifteen days, has given good results. **Fuchsin** has been highly rec-

ommended as an effective drug in reestablishing the menstrual flow.

Electricity is of great value, faradism, static electricity, galvanism, and galvanic intra-uterine pessaries being applicable according to the nature of the case.

Extract of cows' ovaries fresh corpus luteum has been used with success, (see ANIMAL EXTRACTS: Ovarian Organotherapy).

> The writer reports 20 cases treated by hypodermic injections of **pituitrin** or **hypophysin.** He has seen no bad effects, and a sufficient number of cases have been cured or improved to make the treatment worth trying. Rushmore (Boston Med. and Surg. Jour., Mar. 2, 1916).
>
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AMIDOACETPHENETIDIN HYDROCHLORIDE. See PHENOCOLL HYDROCHLORIDE.

AMINOFORM. See HEXAMETHYLENAMINE.

AMMONIA. — Ammonia, chemically NH_3, is made in large quantities from coal gas by heating the ammoniacal liquor with calcium hydroxide, thus conducting the gas formed through tubes containing charcoal. It may be conveniently obtained in smaller amount by heating an ammonium salt, such as ammonium chloride, with dry caustic soda (sodium hydroxide) or slaked lime (calcium hydroxide). It can be formed by the direct union of nitrogen and hydrogen under the electric spark, and is widely produced in nature through the putrefaction of albuminous substances.

PROPERTIES.—Ammonia is a transparent, colorless gas, having an extremely pungent odor and acrid taste. It is strongly alkaline in reaction, and

dissolves very readily (to the extent of 700 volumes) in water, forming a strong solution designated as ammonium hydroxide (sp. gr., 0.897 at 25° C., U. S. P.).

PREPARATIONS AND DOSE.—

The preparations of ammonia included in the U. S. Pharmacopœia are as follows:—

Aqua ammoniæ (ammonia water, hartshorn), containing 10 per cent. by weight of ammonia gas; dose, 10 to 30 minims (0.6 to 2.0 c.c.).

Aqua ammoniæ fortior (stronger ammonia water), containing 28 per cent. by weight of ammonia gas; used chiefly externally as a vesicant.

Spiritus ammoniæ (spirit of ammonia), an alcoholic solution, containing 10 per cent. of ammonia; dose, 10 to 30 minims (0.6 to 2.0 c.c.).

Spiritus ammoniæ aromaticus (aromatic spirit of ammonia), composed of ammonium carbonate, 34 parts by weight; ammonia water, 90 parts by volume; oil of lemon, 10 parts; oils of lavender flowers and of nutmeg, of each, 1 part; alcohol, 700 parts; water, enough to make 1000 parts. A nearly colorless liquid when fresh, but gradually becoming darker; dose, 30 to 60 minims (2.0 to 4.0 c.c.).

Linimentum ammoniæ (ammonia liniment), composed of ammonia water, 350 parts by volume; alcohol, 50 parts; cottonseed oil, 570 parts; oleic acid, 30 parts. Should be freshly prepared when wanted.

The following non-official preparations have also occasionally been used:—

Fetid spirit of ammonia, composed of asafetida, 1 part; spirit of ammonia, 21 parts; dose, 30 minims (2.0 c.c.).

Camphorated ammonia liniment, composed of ammonia water, 30 parts; camphor liniment, 70 parts.

Ointment of ammonia, composed of ammonia water, 17 parts; lard, 32 parts; oil of sweet almonds, 2 parts.

MODES OF ADMINISTRATION.—

Ammonia is miscible in all proportions with water and alcohol. The most agreeable preparation for internal use is the aromatic spirit, which should always be given well diluted with water. As a stimulating inhalation, the gas arising from ammonium carbonate (the ordinary "smelling salts") is frequently employed; but this may readily be replaced by the simple ammonia water, or, if additional care is used, by the stronger ammonia water. The spirit and the water of ammonia have also been administered hypodermically, or even intravenously, as stimulants, though their action is but fleeting, and considerable local irritation, may arise. In pneumonia and other dyspneic states a little ammonia water dropped into boiling water at frequent intervals will "soften" the atmosphere and greatly facilitate breathing.

Externally, the stronger ammonia water may be applied in full strength as a vesicant, and the area under treatment should be covered with a watch-glass to prevent evaporation. For counterirritant effects, a 10 per cent. aqueous preparation, such as the weaker ammonia water, or a stronger oily preparation, such as the official ammonia liniment, is suitable. In children with delicate skins these preparations should be further diluted. In spasmodic croup a little ammonia added to water and applied to the child's neck and chest by means of a cloth will often bring considerable relief, though much care is required to have the fluid sufficiently dilute and not to leave it on too long. The evanescence of the effects of ammonia resulting from its volatility requires

that its administration be frequently repeated.

INCOMPATIBLES.—Mineral or vegetable acids and acid salts, which ammonia neutralizes with the formation of neutral salts; salts of the alkaloids, which ammonia may cause to be precipitated by combining with the acid radical (thereby setting free the more or less insoluble pure alkaloid); chlorine, bromine, and iodine, with which ammonia combines to form corresponding salts; mercurial and most other metallic salts, with which ammonia forms insoluble mixed salts or hydroxides.

CONTRAINDICATIONS.—In acute inflammations of the stomach and in cases where the urine is abnormally acid the internal use of ammonia is to be avoided. In small children and in persons with a sensitive respiratory tract, the inhalation of ammonia fumes is likewise apt to be prejudicial, large amounts giving rise to a bronchitis.

PHYSIOLOGICAL ACTION.— Local Effects.—Solutions of ammonia strongly irritate any tissues with which they may be brought in contact. Applied to the skin, they act as rubefacients or vesicants, according to the concentration of the preparation used and the length of time it is left on the tissues. On the mucous membranes, especially the conjunctivæ, the buccal and the respiratory mucosæ, ammonia vapor acts primarily as a stimulant, exciting the local nerve-terminals, causing increased flow of glandular secretions, and, when concentrated, spasm of the glottis; when kept in contact for a longer time, ammonia preparations cause inflammatory changes which may result in local death of the tissues, followed by sloughing. The caustic action of ammonia is due, as is the case with other alkalies, to a combination with the tissue albumins, resulting in the formation of alkali albuminates, and with the fats to form soaps. The great penetrating power of ammonia, due to its volatility, renders it, when concentrated, one of the most deeply acting of corrosives.

Effects on Internal Use.—*Nervous System.*—After being absorbed into the circulation, ammonia stimulates, for a short period, the medulla oblongata and the motor side of the spinal cord. The higher brain-centers are, if anything, slightly depressed. The spinal stimulation results in an exaggeration of reflex activity and, with excessive doses, in convulsions. Succeeding the stage of stimulation, a secondary stage of depression of the medullary centers and spinal cord may occur with large doses.

Circulation.—Ammonia stimulates the heart muscle, the vasomotor center in the medulla, and, to a less extent, the inhibitory (vagus) center, likewise in the medulla. These effects result mainly in a pronounced rise of the general blood-pressure. The heart beats more strongly, but its rate is frequently slowed. Excessive doses may lead to a secondary depression of both the heart and vasomotor mechanism.

Respiration.—The respiratory centers in the medulla are strongly stimulated by ammonia. Both rate and depth of breathing are increased through its action.

Secretions.—Ammonia and the ammonium compounds stimulate the flow of body secretions, especially the sweat, saliva, and mucous secretions. The diaphoretic effect is believed to be wholly central, *i.e.*, due exclusively to excitation of the sweat-center in the medulla. The other secretory effects are ascribed both to a central action and to a local effect on the gland-cells.

Digestive Tract.—Moderate doses of ammonia stimulate, like other alkalies, the gastric glands if taken before meals. After meals they neutralize the acids of the gastric juice. Large amounts of ammonia exert a corrosive action on the mucosæ (*v.* Ammonia Poisoning).

Absorption and Elimination.—Concerning the manner in which ammonia exerts its stimulating effect, there are still differences of opinion. Some claim that, after being rapidly absorbed, ammonia, circulating with the blood, stimulates the vital centers directly; others believe that the centers are stimulated mainly reflexly, as a result of the local irritation produced in the stomach.

The researches of Magnus showed ammonia to be neither absorbed nor excreted by the lungs. Hence, in so far as its administration by inhalation is concerned, the stimulating effects of ammonia would appear to be due largely to peripheral sensory stimulation.

When taken internally, on the other hand, ammonia is readily absorbed; but on reaching the blood-stream it rapidly undergoes a chemical change whereby it is converted into the relatively inert substance urea. Whatever direct stimulating action it may exert on the nerve-centers and heart is, therefore, quickly brought to an end.

By the conversion into urea, the ammonium in ammonium hydroxide loses the characteristics of an alkali metal. For this reason ammonia does not increase the alkalinity of the body fluids, differing thus from the hydroxides of sodium and potassium, which cannot undergo the change referred to.

The urea produced from the ammonia is naturally eliminated largely with the urine, which may be somewhat increased in amount owing to stimulation of the renal cells by the excess of urea.

TOXICOLOGY.—The ingestion of strong solutions of ammonia results in corrosion or violent inflammation of the mucous membranes of the mouth, esophagus, and stomach, and in marked irritation of the larynx and trachea, owing to the penetration of ammonia vapor into the respiratory passages. The symptoms consist of violent pain in the mouth, throat, and abdomen; salivation; vomiting, sometimes bloody, and, occasionally, purging. The intense irritation of the respiratory mucous membranes may cause, at first, a momentary arrest of breathing and depressed heart action, as well as spasmodic contraction of the laryngeal and bronchial muscles. Later, the persisting laryngeal irritation causes intense local burning and a characteristic difficulty of respiration, due to actual edematous swelling of the glottis. Sudden death by asphyxia may result, though more frequently it is due to shock arising from the pronounced local destructive effects of the alkali, or to collapse, possibly owing to a secondary depressive effect of the drug on the heart and medullary centers. Convulsions, however, are comparatively infrequent in ammonia poisoning, and this fact would tend to indicate that in the majority of cases the amount of ammonia absorbed is insufficient to cause violent direct effects on the nerve-centers.

The ultimate results in cases of ammonia poisoning can seldom be predicted with certainty. Not only may laryngeal or bronchial inflammation follow, but the gastric mucosa may be so greatly injured as permanently to impair the functions of the stomach, and even cause death from inanition. Moreover, in cases that recover from the acute effects, stricture of the esophagus is a frequent sequela. As with other

caustics, the upper and lower extremities of the gullet and the point at which it crosses the left bronchus are the favorite seats of corrosion.

Large doses of ammonia (providing a sufficient amount is absorbed) are said to diminish the oxygen-absorbing power of the red blood-corpuscles and to interfere with coagulation.

Treatment of Ammonia Poisoning. —The chief ends to be sought in the treatment of the first stage of the poisoning are neutralization, dilution, and removal of the obnoxious agent. **Vinegar, lemon juice,** or any other available acid (preferably a vegetable acid), well diluted, should be given, together with a large amount of water. Where no acid is at hand, an oil, such as **olive oil** or **linseed oil,** forms the best substitute. The **stomach-pump** may then be cautiously used, though, if sufficient time for marked corrosion of the tissues has already elapsed, its passage is attended with some danger, owing to the liability of the weakened tissues to perforation.

Morphine should be given if the pain is severe, and **tracheotomy** may be required if asphyxia threatens.

If symptoms of shock or secondary collapse appear, the usual measures for combating these states — hypodermic injections of **ether, digitalis, atropine, strychnine; hot, strong coffee** by the rectum; **external heat, artificial respiration,** etc.— should be availed of.

Demulcents, such as **olive oil, starch paste, tragacanth mucilage, milk, white of egg,** or an infusion of **elm bark,** should be freely administered to soothe the inflamed mucous membranes. No food is to be given by the mouth for two days after the accident.

Strictures of the esophagus should be treated by **dilatation with bougies** (*v.* Esophagus, Stricture of).

APPLIED THERAPEUTICS OF AMMONIA.—As a Stimulant.—Ammonia is of great value as a rapidly acting "diffusible" stimulant, exerting a marked beneficial effect in all forms of **acute circulatory, respiratory,** and **nervous depression.** It may be administered either by the mouth, by inhalation, or by hypodermic or intravenous injection. For internal use, the aromatic spirit of ammonia, always well diluted, in doses of 15 minims to 1 dram (1 to 4 c.c.), is the best preparation. For inhalation, ordinary ammonia water, or "smelling salts," may be used. The effect of ammonia, when it is taken internally, is believed by some to be chiefly reflex, varying in intensity with the degree of local irritation produced. A similar mode of action is known to obtain when ammonia is inhaled; none of it is absorbed through the lungs, and the effect is correspondingly fugacious. The true stimulating effect of ammonia is best obtained by intravenous injection, though the hypodermic method is oftener employed.

In **asphyxia,** whatever be its origin, ammonia is a valuable agent. It may, with advantage, be given at once internally and by inhalation. During the latter procedure care should be taken not to spill any of the strong liquid into the patient's mouth or nose,—an accident which is likely to occur when the patient is recumbent, and which is apt to yield a more pronounced effect, however, than its ingestion.

In cases of **sudden heart-failure** or **collapse,** as may result from the presence of bacterial toxins or poisoning by depressant drugs, such as hydrocyanic acid, chloroform, chloral hy-

drate, aconite, etc., repeated ingestion of 15 minims to 1 dram of the aromatic spirit of ammonia, diluted with half a tumblerful of water, or the intravenous injection of like amounts of ammonia water, diluted with 6 drams of sterile water, will usually exert a powerful stimulating action. Ammonia may likewise be used internally to combat the effects of **bites of poisonous animals.**

In ordinary "fainting" and the lighter forms of **shock,** the inhalation of ammonia from its solution or from smelling salts may suffice to bring about the desired result.

In infants, collapse occurring in **summer diarrhea** may be combated with occasional doses of a few drops of ammonia, well diluted.

For the algid stage of **cholera,** ammonia internally and ether hypodermically, with simultaneous free administration of alcohol, have been highly recommended by Giacich. Marked improvement in the general condition was noted within two hours after the institution of this mode of treatment, and over 50 per cent. of cases already in the algid stage are said to have recovered.

In **acute alcoholic intoxication,** the ammonia preparations are considerably used. Lavage of the stomach, followed by the administration of 10 drops of ammonia water in a half-tumblerful of water, will often counteract promptly the effects of the alcohol. Ammonia has also been used with benefit in the treatment of **delirium tremens** (Butler).

As an Antacid.—Internally, ammonia may be used to counteract **gastric hyperacidity,** indicated by such symptoms as acid eructations ("heartburn") and flatulence. Par-

ticularly where there are pronounced abnormal fermentative processes, resulting in the formation of vegetable acids, does ammonia appear to be efficient. A few drops (3 to 5) of the water of ammonia, or 10 drops of the aromatic spirit, well diluted, will often give relief under these circumstances. It should be remembered that, although the ammonia introduced will tend to neutralize any acids present, the local irritation produced by it will, in addition, tend to stimulate the gastric glands and musculature. Hence the special degree of benefit obtained where there is **flatulence** and in cases where the gastric functions are weakened by **general debility** or **excessive alcoholic indulgence.**

In **poisoning by mineral acids,** such as hydrochloric or sulphuric acids, well-diluted ammonia may be given as an antidote (though a less-irritating alkali, when at hand, is much preferable).

Externally, in painful **insect bites,** ammonia may be used to neutralize the acid (frequently formic acid) introduced at the moment of stinging. Its antiseptic action is also helpful.

As a Counterirritant, Rubefacient, or Cauterant.—Ammonia water applied to the skin acts powerfully in relieving subjacent pain, though the superficial pain attending its use is not infrequently more severe than is the case with other counterirritants.

In patients with kidney affections, in particular, it has been used as a vesicant in place of cantharides, which causes harmful renal irritation in these cases. It has the property of passing through the horny layer of the epidermis without destroying it (as would other strong alkalies), and of inducing blister formation through irritation of the dermis.

In **bruises, chilblains,** and other superficial lesions, ammonia liniment may be employed as a rubefacient. It sometimes relieves the milder forms of **chronic rheumatism,** including the joint manifestations and **lumbago.**

The corrosive and antiseptic properties of ammonia may be utilized with great advantage and convenience in treating the **bites of carnivorous animals, venomous reptiles and insects.** In snake-bites, for example, strong ammonia water may be applied directly to the wound, the general stimulating effect of ammonia being also availed of by giving an intravenous injection of 30 to 60 minims of the weaker solution in 6 drams of sterile water. In insect stings, the local application of ammonia water will often greatly reduce the pain or itching; especially where a tendency to local infection exists, the antiseptic property of the remedy may be utilized with great benefit. The patient should always be cautioned, however, to remove the ammonia when marked redness of the skin appears; otherwise, considerable local injury is likely to result. In a case witnessed by the writers, the patient had used it in the form of a compress to treat a horse-fly bite. The large area thus "treated" resembled a burn of the second degree. Most people handle ammonia carelessly.

In the "hair tonics" recommended in premature **alopecia,** ammonia water is considered a valuable ingredient. The aromatic spirit of ammonia is also used in various other affections of the scalp, including **pityriasis,** etc.

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AMMONIUM. —A metal-like body, never yet isolated in pure form, but known, from the manner in which its compounds can be formed by the interaction of ammonia gas and acids, to have the chemical composition NH_4. The compounds of ammonium greatly resemble those of potassium; hence the inclusion of ammonium in the group of alkali metals. The official salts of ammonium are the following:—

Ammonii benzoas (ammonium benzoate); dose, 5 to 30 grains (0.3 to 2.0 grams).

Ammonii bromidum (ammonium bromide); dose, 5 to 30 grains (0.3 to 2.0 grams).

Ammonii carbonas (ammonium carbonate); dose, 2 to 15 grains (0.12 to 1.0 gram).

Ammonii chloridum (ammonium chloride); dose, 2 to 30 grains (0.12 to 2.0 grams).

Ammonii iodidum (ammonium iodide); dose, 3 to 15 grains (0.2 to 1.0 gram).

Ammonii salicylas (ammonium salicylate); dose, 3 to 15 grains (0.2 to 1.0 gram).

Ammonii valeras (ammonium valerianate or valerate); dose, 2 to 10 grains (0.12 to 0.6 gram).

Ammonium acetate is official in *liquor ammonii acetatis* (spirit of Mindererus), a solution of diluted acetic acid nearly saturated with ammonium carbonate; dose, 4 fluidrams (16 c.c., containing about 15 grains or 1 gram of ammonium acetate), and in *liquor ferri et ammonii acetatis* (Basham's mixture), which is made up of tincture of ferric chloride, 1 fluidram (4 c.c.); diluted acetic acid, 1½ fluidrams (6 c.c.); solution of ammonium acetate, 12½ fluidrams (50 c.c.); aromatic elixir, 3 fluidrams

(12 c.c.)'; glycerin, 3 fluidrams (12 c.c.), and water, enough to make 25 fluidrams (100 c.c.) ; dose, 4 fluidrams (16 c.c.).

PHYSIOLOGICAL ACTION.— The effects of the compounds of ammonium are a composite of those of the ammonium group or ion itself, and of the acid group in union with it. The latter may not only modify that of the ammonium, as in ammonium bromide, but may completely overshadow it, as in ammonium arsenate.

The effects of the ammonium ion, when it enters the circulation, are, in general, those of a promptly acting, but fleeting stimulant. If the amount introduced be excessive, depression may follow the primary stimulation.

In the *nervous system* the stimulating effects of ammonium bear chiefly upon the spinal cord and medulla. The motor spinal centers are excited to increased activity, exaggerated reflex action, and even convulsions, being among the most evident results. The cerebrum, however, is, if anything, depressed rather than stimulated. The *circulation* is influenced in various ways: 1. Stimulation of the vasomotor center in the medulla causes a rise of blood-pressure through constriction of the peripheral blood-vessels. 2. The heart muscle is directly stimulated, the result being a strengthening of its beats and further rise in the blood-pressure. 3. Excitation of the vagus (inhibitory) center in the medulla may cause some slowing in the heart rate. *Respiration* is accelerated and deepened through stimulation of the medullary centers presiding over this function. The *body secretions,* especially the sweat, saliva, and mucous secretions of the alimentary and respiratory tracts, are in-

creased by ammonium, partly through stimulation of the nervous centers governing secretory processes (exclusively so in case of the sweat secretion), and partly owing to local effects on the secreting cells.

Though most of the ammonium compounds are readily and promptly absorbed from the stomach and intestines, their excretion through the urine and other secreted fluids is so rapid as to greatly limit the power and duration of their effects when taken by the mouth. Further, certain of the salts of ammonium, *i.e.,* the acetate and citrate, when absorbed, are oxidized to ammonium carbonate in the system, and this, in turn, undergoes a rapid decomposition, probably mainly in the liver, whereby it is converted into urea. The ammonium group is thus destroyed, and its specific effects promptly disappear. Only by intravenous injection of rather considerable amounts of ammonium salts are the effects of the NH_4 group obtained with any degree of intensity.

The decomposition of the NH_4 group into urea involves loss of the alkaline properties of its compounds. For this reason the alkalinity of the blood is not increased and the acidity of the urine not diminished by the administration of alkaline salts of ammonium, as they would be by giving alkaline salts of sodium and potassium.

Ammonium salts which are not changed to the carbonate and eliminated as urea—*e.g.,* ammonium chloride—are excreted as neutral salts, and, therefore, also fail to influence the reaction of the urine.

The contrast between the stimulating action of ammonium hydroxide (ammonia) or ammonium carbonate and the almost complete absence of it in the case of ammonium chloride is now be-

lieved to be due not to any greater rapidity of absorption or more prolonged persistence of ammonium in the blood (the reverse being, in reality, the case), but to the reflex stimulation caused by the caustic alkaline action of the first-mentioned two compounds on the gastric mucosa (or wherever else brought into relation with the organism), as compared to the low degree of local irritation caused by the practically neutral chloride of ammonium.

As already mentioned, some of the ammonium compounds owe their therapeutic value chiefly to the acid group—benzoate, bromide, salicylate, etc.—with which the ammonium is in combination. For information concerning these the reader is referred to the headings under which the respective acids are considered: **Benzoic acid, bromides, salicylic acid,** etc. The more important of the compounds in the physiological action of which the ammonium group plays the leading part will be treated of in the following sections.

AMMONIUM ACETATE.—Ammonium acetate ($CH_3 . COONH_4$) occurs as a white crystalline solid, freely soluble in water. It is seldom used in its natural state, but enters into the composition of the official *liquor ammonii acetatis* (spirit of mindererus), which is extensively employed. This fluid is prepared by neutralizing dilute acetic acid with ammonium carbonate (5 grams of the former in 100 c.c. of the latter, according to pharmacopeial directions), the result being a colorless liquid, which may give off a faint odor of acetic acid, and has a mildly saline, acidulous taste and an acid reaction. The preparation is required to contain not less than 7 per cent. of ammonium acetate, and should be freshly prepared

when wanted. The **dose** of spirit of mindererus is 2 fluidrams to 1 ounce (8.0 to 30.0 c.c.), repeated every two or three hours.

Liquor ferri et ammonii acetatis (Basham's mixture) will be considered among the preparations of iron.

MODE OF ADMINISTRATION. —Liquor ammonii acetatis is best administered well diluted in sweetened water. Sparkling water (charged with carbon dioxide) is also advantageous as a diluent.

INCOMPATIBLES.—Strong acids, which enter in combination with the ammonium, replacing the weaker acetate radical; compounds of bases stronger than ammonium (sodium, potassium), with acids weaker than acetic acid, *e.g.*, the carbonates of sodium and potassium; lime water (calcium hydroxide); metallic salts, such as those of silver and lead.

PHYSIOLOGICAL ACTION. — Ammonium acetate, especially when given in the official solution, is the most strongly *diaphoretic* of the salts of ammonium. Its action is believed to take place largely, if not solely, through stimulation of the sweat-center. The diaphoresis occurring under its influence is greatly assisted if the cutaneous vessels are already in a state of dilatation or are caused to dilate by the application of warmth—blankets—to the patient's skin, or by combination with sweet spirit of niter or aconite.

A second useful property of this salt is its action as a *diuretic*. This action is exerted most strongly when diaphoresis is held in abeyance, *i.e.*, when the skin vessels are not dilated. The diuretic effect of ammonium acetate is not produced through irritation of the kidney-cells. This is one of the ammonium salts which are rapidly con-

verted in the system, first into ammonium carbonate, then into urea; hence the diuretic effect is probably chiefly that of urea,—a normal stimulant to the renal function.

Ammonium acetate is believed to be one of the most rapidly absorbed of the ammonium salts; we should, therefore, expect that some of the stimulating action of ammonium on the medullary nerve-centers and circulation would be exerted on ingestion of this salt. Such stimulation does not, however, with the exception of the sweat-center, appear to occur to any marked extent. The reason for the special preponderance of diaphoresis in the action of this salt of ammonium is not definitely known.

THERAPEUTICS.—As a Diaphoretic and Diuretic.—The solution of ammonium acetate is useful as a mild sweat-producer and diuretic in febrile diseases, including **acute coryza, influenza, mumps,** the **eruptive diseases of childhood,** etc. The elimination of toxic products, in which the skin, as well as the kidneys, plays so important a part in these affections, is hastened by it. It also tends to reduce excessive temperatures by increasing the amount of fluid evaporated from the skin. In the diseases of childhood, when the eruption is delayed, ammonium acetate will favor its appearance. It has also been found serviceable in **muscular rheumatism** (Butler).

In **acute alcoholic intoxication** ammonium acetate has been found to remove promptly the symptoms. In **migraine,** too, through some obscure mode of action, and in **amenorrhea,** the remedy has sometimes proved beneficial (Butler).

Externally, solutions of ammonium acetate have been applied as a lotion over **contusions, beginning abscesses** and **glandular enlargements,** and certain skin diseases, e.g., **prurigo.** In **chronic ophthalmic inflammations,** also, it has been used as an eye-wash, a little laudanum being added to the acetate solution in order to relieve local discomfort.

AMMONIUM CARBONATE.— The substance used under this name is not the pure carbonate of ammonium, $(NH_4)_2CO_3$, but is a mixture in variable ratio of acid ammonium bicarbonate, $(NH_4)HCO_3$ or $CO(OH)ONH_4$, and ammonium carbamate, $CO(NH_2)ONH_4$. This mixture is also known as ammonium sesquicarbonate, hartshorn, sal volatile, Preston salts, or bakers' ammonia. It is made by heating an ammonium salt, such as the chloride, with chalk (calcium carbonate), and occurs in white, hard, translucent masses having a sharp, saline taste, a strong odor of ammonia, and a strongly alkaline reaction to litmus. It loses both ammonia gas and carbon dioxide when exposed to the air, and effloresces, becoming opaque and friable. When heated it volatilizes completely. When dissolved in hot water it is decomposed, ammonia and carbon dioxide being driven off; upon further boiling it disappears from the solution by volatilization. It is soluble in 5 parts of water at a temperature of 15° C. (59° F.), and in 4 parts at 25° C. (77° F.). Alcohol dissolves only its carbamate constituent, the acid carbonate remaining. In glycerin it is soluble to the extent of 1 in 5 parts. The purity standard set for ammonium carbonate by the United States Pharmacopœia is that it should contain 97 per cent. of the constituents above mentioned, and should yield not less than 31.58 per cent. of ammonia gas.

The dose of ammonii carbonas is 2 to 15 grains (0.12 to 1.0 gram), the average being 5 grains (0.3 gram).

The aromatic spirit of ammonia (*spiritus ammoniæ aromaticus*), already considered under ammonia (*q.v.*), contains about 4 per cent. of ammonium carbonate.

MODE OF ADMINISTRATION. —Ammonium carbonate should not be given in any form other than a well-diluted solution, thus avoiding excessive gastric irritation and facilitating absorption. The evanescence of the effects of this salt, in common with other ammonium salts, requires that it be frequently repeated, *e.g.*, every two hours. Its unpleasant taste may be covered by licorice.

INCOMPATIBLES.—Ammonium carbonate is incompatible with acids, with acid salts, and with lime water.

PHYSIOLOGICAL ACTION.— Ammonium carbonate possesses, to a certain extent, the stimulating properties of ammonia. As has already been stated, the general stimulant effect of the latter, taken internally, is now believed due not so much to a direct action of the ammonium group on the nerve-centers and circulation after absorption as to the irritation of the gastric mucous membrane due to the strong alkalinity of ammonia. The same view is held with regard to ammonium carbonate, the lesser extent of its stimulating effect corresponding with its lower degree of alkalinity as compared to ammonia. Taken in considerable amounts, the salt causes vomiting.

If ammonium carbonate is injected subcutaneously or intravenously, direct stimulation of the respiratory and vaso-motor centers, spinal cord, and heart by the ammonium circulating in the blood (in addition to the reflex stimulation from local irritation, when injected subcutaneously) is produced.

Like the acetate of ammonium, the carbonate acts as a mild diaphoretic and diuretic. It possesses also, to a considerable degree, the property of increasing the bronchial secretions and mucus in general. After absorption it is partly oxidized to urea; but some of it is excreted unchanged by the bronchial and other glands, which are stimulated by it. According to Sollmann, ammonium salts in increasing secretions of the respiratory tract and the saliva act in no less than four ways: 1. By reflex stimulation from the mucous membranes with which the salt is brought in contact. 2. By direct stimulation of the secretory nerve-centers, which the drug reaches through the circulation. 3. By a local stimulating action on the gland-cells themselves, with the secretions of which the salt is excreted. 4. Through liquefaction of the mucous secreted, owing to the alkalinity of the ammonium carbonate eliminated with it. (Several ammonium salts, besides the carbonate itself—the acetate, citrate, etc.—are converted in the system into, and partly eliminated as, the carbonate.)

Ammonium carbonate, like ammonia, is, to a certain extent, antiseptic, owing to its alkalinity. Applied to the skin, it acts as a rubefacient.

The pure neutral carbonate of ammonium—$(NH_4)_2CO_3$—is of physiological importance. The nitrogenous waste product of the activity of muscles is ammonium lactate. This, according to the belief of some, is converted in the tissues into ammonium carbonate, which, in turn, is dehydrated in the liver to ammonium carbonate, and, finally, to urea. Where the hepatic functions are deficient, ammonium car-

bonate or carbamate may persist, and cause symptoms of ammonium poisoning, somewhat resembling those of uremia.

TOXICOLOGY.—Ammonium carbonate, ingested in large amount, brings about nausea and vomiting through local irritation. If brought in contact with the mucous membranes in concentrated form, destructive lesions, somewhat similar to those produced by ammonia, may result. For symptoms and treatment the reader is referred to the section on the toxicology of ammonia.

THERAPEUTICS.—As an **expectorant,** ammonium carbonate is of considerable value. The secretions are both increased and rendered more fluid, being, therefore, removed with greater facility. In **bronchitis, pneumonia, asthma,** and **pulmonary tuberculosis,** the combination of the expectorant effect with the stimulating action on the respiratory centers is very advantageous, more especially in cases where dyspnea is marked. In these affections it should be given in doses of 5 or 10 grains (0.3 to 0.6 gram), repeated every two hours.

In **acute coryza** it may also be employed with satisfactory results.

As a Stimulant.—The stimulating effect of this remedy on the medullary centers and heart is of great value in all conditions of general adynamia, with or without involvement of the respiratory tract. In the **acute exanthemata** of children, and **continued fevers** of various kinds, it may be used with great advantage to sustain circulatory and respiratory activity. In **bronchopneumonia, chronic bronchitis** with marked general weakness, it is a favorite remedy. In **chronic heart disease** with failure of compensation it is also frequently used. The

effect is, of course, of brief duration, and frequent administration being required to keep up the action. In **"fainting" (syncope)** and **shock** the inhalation of "smelling salts" (ammonium carbonate reinforced with ammonia water) is a time-honored and effective procedure.

As a Gastric Stimulant or Emetic. —In **indigestion** due to **general weakness,** and in cases where **flatulence** is a prominent symptom, ammonium carbonate may be used to tone up the gastric functions. Its effects are, however, evanescent. In the **indigestion of alcoholics** it has also proven very useful.

Emesis may be obtained by the administration of large doses, *e.g.,* 30 grains (2 grams), of ammonium carbonate. The absence of concomitant depressing effects distinguishes this form of emesis from that caused by depressing drugs, such as tartar emetic.

As a Rubefacient and Discutient.— Ammonium carbonate may be employed as a rubefacient in a manner similar to ammonia (*q.v.*). In **psoriasis,** baths containing ammonium carbonate are given for the purpose of dissolving off the scaly coverings of the lesions, in order that the local remedies subsequently applied may act directly on the skin.

AMMONIUM CHLORIDE, also known as "sal ammoniac" or muriate of ammonia, has the chemical formula NH_4Cl. It may readily be produced by the interaction of ammonia and hydrochloric acid, but is more usually produced by neutralizing ammonia with sulphuric acid, separating by crystallization the ammonium sulphate thus formed, and subliming it with sodium chloride. It occurs as a white, crystalline powder, odorless, but having a cool-

ing, saline taste. In contrast with ammonium carbonate, ammonium chloride is permanent in the air. When strongly heated it is completely volatilized, without decomposition.

Ammonium chloride is soluble in 2 parts of water, in 50 parts of alcohol, and in 5 parts of glycerin at 25° C. (77° F.), and in 1 part of boiling water. Though ammonium chloride is a neutral salt, its solution in water has a slightly acid reaction. This is due to the fact that small amounts of NH_4OH and of HCl are formed in the solution by reaction of NH_4Cl with H_2O, and that the HCl is dissociated into its ions to a greater degree than the NH_4OH, therefore being chemically more active and producing the acid reaction.

The dose of *ammonii chloridum* is 2 to 30 grains (0.12 to 2.0 grams), the average being 7½ grains (0.5 gram). The *trochisci ammonii chloridi* (troches or lozenges), also official, each consist of ammonium chloride, 0.1 gram (1½ grains); extract of glycyrrhiza, 0.2 gram (3 grains); tragacanth, 0.02 gram (⅓ grain); sugar, 0.4 gram (6 grains), with syrup of Tolu, q. s.

MODES OF ADMINISTRATION.—Ammonium chloride is best given in solution or in the form of lozenges. Licorice is decidedly the most advantageous agent for disguising its unpleasant salty taste. The *mistura ammonii chloridi* of the National Formulary, *e.g.*, contains 2½ parts each of the salt and of pure extract of licorice in 100 parts of water. Similarly, the *mistura glycyrrhizæ composita* (brown mixture) of the U. S. P. is often used as a vehicle for ammonium chloride. In affections of the lower respiratory passages inhalations of freshly formed ammonium chloride vapors are also frequently utilized.

INCOMPATIBLES.—Ammonium chloride is incompatible with alkaline compounds or carbonates of the stronger alkali metals,—sodium and potassium,—or of the metals of the alkaline earths,—calcium, strontium, barium; the more strongly basic metals in these compounds tend to displace the ammonium from its chloride. If an ammonium chloride solution to which sodium or potassium hydroxide has been added is heated, gaseous ammonia is evolved. Salts of silver, mercury, or lead, in solution, are precipitated as insoluble chlorides if combined with the chloride of ammonium.

PHYSIOLOGICAL ACTION.—Taken internally, ammonium chloride, being less irritating than ammonia or ammonium carbonate, causes but little reflex irritation of the central nervous system through irritation of the gastric mucosa. In view of the fact, however, that it is destroyed in the blood to a much less extent than ammonium carbonate and ammonium acetate (which, as has already been stated, are largely converted to the relatively inert substance, urea), we would expect ammonium chloride to exhibit the direct stimulating effect of ammonium on the nerve-centers more clearly than the compounds just mentioned. That this is not the case, ammonium chloride being but slightly a general stimulant, tends to support the view, now held by many, that the stimulating effects of ammonium compounds taken internally are exerted through a reflex, rather than a direct, action on the centers. Nevertheless, if the salt be given intravenously, the direct stimulating action of ammonium on the spinal cord, the respiratory, vasomotor, and other centers, as well as the heart muscle, becomes clearly manifest. It may be pre-

ceded by a period of central nervous depression, as was well illustrated in the results obtained by Gourinsky in experiments on frogs and pigeons. His findings were these: In frogs whose spinal cord has been divided below the medulla oblongata ammonium chloride produces, from the first, a marked augmentation of reflex action. In normal frogs and pigeons, on the other hand, ammonium chloride produces, at first, depression of the central nervous system, then convulsions; the higher centers at first exercise an inhibitory influence on the spinal reflexes. When the salt is introduced rapidly, the first stage (that of depression) is but slightly marked, and soon gives place to the second stage (that of irritation, ushered in by convulsions). When it is introduced slowly the depression is well marked and lasts a long time. In frogs and pigeons deprived of the cerebral hemispheres only, whatever be the method of introducing the salt, convulsions are not preceded by depression, but the latter is sometimes replaced by irritability. All the facts, according to Gourinsky, can be explained only by the reciprocal action of the nervous centers on each other, modified by the ammonium chloride. It should be mentioned, in this connection, that, in the frog, ammonium chloride has a tendency to paralyze the motor nerve-terminals in the muscles; in mammals, however, this effect is hardly noticeable, even with large doses.

The most important action of ammonium chloride is that on the secretions of the respiratory passages, stomach, and mucous membranes in general, which are increased and rendered more fluid by it. The several ways in which this effect may be produced have been set forth under ammonium carbonate (q.v.). The fact that some of the salt is eliminated by the mucous membranes suggests that the direct action of the drug on the gland-cells must play an important rôle in the effect produced. Its elimination with the sweat and urine also causes it to be mildly diaphoretic and diuretic, as well as expectorant.

Ammonium chloride has been found to produce an increase in all the solids of the urine, except in uric acid.

When given continuously for some time, it is believed to cause pathological alterations in the blood, which may eventuate in general prostration, together with hemorrhage under the skin, from the mucous membranes, and hematuria.

Externally, ammonium chloride, in strong solutions, acts as an irritant.

THERAPEUTICS.—As a Stimulant to Mucous Membranes.—*In Disorders of the Respiratory Tract.*—Ammonium chloride has long been considered an effective remedy in almost every disorder of the respiratory tract. More recently the carbonate has replaced it in the treatment of pulmonary disorders, but the chloride is still widely used in **chronic bronchitis** and **acute bronchitis** after the initial stage of the bronchial inflammation has passed that of marked congestion and dryness. In **whooping-cough,** also, ammonium chloride has given fairly good results. The drug acts, at least in part, directly on the gland-cells of the mucous membranes, with the secretions of which it is eliminated into the bronchi. The cells are stimulated by virtue of its "salt action," the result being a less tenacious and more watery secretion of mucus, which is more readily evacuated. Frequently the drug is given in combination with other stimulating expectorant remedies. In the terminal stage of

acute coryza and in subacute or chronic forms of pharyngitis and laryngitis, the beneficial effects of ammonium chloride on the mucous membranes are also utilized with advantage.

In **pneumonia,** ammonium chloride has been given in 10-grain (0.6 gram) doses every two hours, in the hope of in some way favorably modifying the inflammatory process in the lung, but the results obtained have not been striking (Brunton).

Fumes of nascent ammonium chloride, generated by the action of hydrochloric acid on ammonia, are frequently administered by inhalation in respiratory disorders, and have proven quite effective in mild chronic affections of the mucous membranes, including **bronchitis, pharyngitis, laryngitis,** etc.

It is a constituent of the official *mistura glycyrrhizæ composita* (U. S. P.), of mistura ammonii chloridi (N. F.).

The value of ammonium chloride troches, or lozenges, for local stimulation in **pharyngeal disorders** is well known. They serve the double purpose of increasing local lubrication by exciting the glandular acini and of gently stimulating the hepatic functions after the salt has been absorbed. The official ammonium chloride lozenge has already been referred to; 1 to 6 or more of these lozenges may be taken daily.

Ammonium chloride solution has also been used in throat affections in the form of a spray.

In Aural Disorders.—The use of chloride of ammonium vapor in affections of the middle ear has been prompted by its effectiveness in catarrhal affections of the nasal mucous membrane.

In Gastric Catarrh.—That ammonium chloride is of value in catarrhal disorders of the stomach, especially in children, is indicated by the frequency with which it is still resorted to. Presumably, its chief action is to loosen the mucous secretions. It may be given in solution or in pills; if in the latter form a half-tumblerful of pure water should be taken simultaneously to prevent undue irritation of the gastric mucosa by the salt. Instead of water, milk may be used.

In Cystitis.—In catarrhal cystitis ammonium chloride sometimes proves very effective. Ten grains (0.6 gram) every four hours on the first day, in a tumblerful of water, and 5 grains (0.3 gram) on the second day and thereafter soon cause the local distress greatly to diminish.

As a Stimulant to the Liver.—In all conditions associated with **torpidity of the liver,** whether this be due to a subacute hepatitis or to general asthenia, ammonia chloride, in doses of 20 grains (1.3 grams) three times a day, has been found of great value.

In Alcoholism.—In alcoholic intoxication ammonium chloride has been said to act as effectively as ammonia. Thirty grains (2.0 grams), repeated in half an hour, were found to bring the sufferer to his normal condition, in so far as the mental aberration was concerned. If emesis or lavage had been resorted to before the administration of the salt, the action of the latter was greatly prolonged.

In Neuralgia and Migraine.—Ammonium has been found frequently to afford considerable relief in these disorders, especially if given with tincture of aconite. Twenty grains (1.3 grams) of the ammonium salt with 2 minims (0.12 c.c.) of the tincture, repeated twice after the first dose, at intervals of half an hour, usually procured marked diminution of the suffering.

External Uses.—In superficial inflammatory swellings, *e.g.*, buboes, mammary abscesses, testicular inflammations, etc., ammonium chloride solutions have been applied locally with benefit.

In **vaginitis** a solution of 3 drams (12.0 grams) of ammonium chloride in 1 pint (475 c.c.) of water can be used as an injection or applied on a tampon with benefit (Butler).

A saturated solution of the salt may be used with advantage in **bruises,** to reduce swelling and diminish discoloration. The antiseptic qualities of ammonium chloride in the treatment of **wounds** have been emphasized by H. C. Wyman, who obtained good results, especially in contused wounds, from the use of gauze steeped in a solution of 1 ounce of the salt in half a pint of water. The circulation of blood in the injured parts also appeared to be improved by it.

In **senile gangrene** a good therapeutic measure is to place the foot in a solution of 8 ounces (250 grams) of ammonium chloride to 1 gallon (3800 c.c.) of water (Butler). It increases the alkalinity of the blood and thereby its osmotic properties, and facilitates its circulation.

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AMMONIUM ICHTHYOL GROUP. See ICHTHYOL.

AMNESIA.—Loss of memory, includes failures of memory of various kinds, both temporary and permanent, or presenting special characteristics, as in the amnesic aphasias. It applies also to a loss of the power to recall facts of every kind, covering a definite period, or the entire life of the subject. In a case following prolonged alcoholic stupor reported by A. C. Buckley (Jour. of Abnormal Psych., Feb.-Mar., 1912), there was a loss of recollection of all events of the life of the individual—he remembered nothing up to a definite point. Nevertheless, he possessed a remarkable degree of tenacity of memory for all events which followed his comparatively abrupt psychic awakening. This was shown by his ability to recall and retain all recent events when once they were brought to his attention. The re-education process was for him a laborious one, covering a period of many months, and to those who had the opportunity to observe him, it was most interesting.

S. P. Goodhart (Jour. Amer. Med. Assoc., Dec. 27, 1913) observed 2 cases of temporary amnesia, 1 from the excessive use of tobacco, the other a result of malarial infection. The first patient was a prominent lawyer and teacher, an habitual user of strong tobacco, who had indulged in unusual excess on account of recent mental and emotional stress. The amnesia appeared suddenly with a dazed condition for a half hour, followed by 3 weeks of nearly complete forgetfulness of past and current events, but apparently without any mental symptoms other than those dependent on the amnesia. Then it gradually began to disappear, but the complete rehabilitation was as sudden as the onset, and seemed to take up the normal mental activity at the point where it had been interrupted. Withdrawal of tobacco, rest and nutritional care were all the treatment used. This was several years ago; since then slight amnesic attacks have followed excessive use of tobacco and have been relieved by similar treatment. The second patient was a female teacher, aged 27, whose mother suffered from epilepsy and who was herself somewhat high-strung and nervous. The attack, in this case, was sudden, after intense emotional strain and fatigue, and was immediately preceded by severe headache. The amnesia was complete for the events of the previous 48 hours, but less so for events more remote. Malarial symptoms appeared two days later, and the case was a typical tertian with finding of the plasmodium. The amnesia continued a prolonged period after malarial symptoms

ceased, and there is yet only partial restoration of past recollections.

Attempts at cure of amnesia by means of **free association** and **hypnosis** were made by Rorschach (Med. Rec., from Correspondenzbl. f. Schweizer Aerzte, July 14, 1917). A soldier sent home on furlough did not return on time. Investigation led to his discovery in a beer cellar in a state of mental confusion and amnesia. Removed to the hospital he was able to remember up to a certain hour on the first day of his furlough when apparently he had met with an accident. He was able to give a good history of himself and family, and had never before been in a twilight state although there may have been an unmotivated tendency in boyhood to wander. He had always been alcohol-intolerant and 2 glasses of beer were enough to rob him of self control. Once he had had an unmotivated attack of weeping. His record as a soldier was good save on one occasion, when he had failed to get up in the morning. When interned he was pale, complained of headache, was alternately euphoric and anxious, and showed numerous peculiarities of behavior. He was first tested with ordinary association (Jung-Riklin) which was at least 93 per cent. internal. Great uniformity was shown, and the total results pointed strongly to epileptic association. Free association tests *per se* could throw no light on the amnesia and the patient was then hypnotized. Under hypnosis certain things were remembered but there were many gaps and posthypnotic suggestion failed completely. It seemed beyond doubt, by the character of the recollections, that during the twilight state patient had been in a delirium which by its content suggested an organic brain disease.   S.

AMPUTATIONS AND RESECTIONS. See RESECTIONS, AMPUTATIONS, ETC.

AMYL NITRITE. See NITRITES.

AMYLENE CHLORAL. See DORMIOL.

AMYLENE HYDRATE. — This substance is chemically tertiary amyl alcohol or dimethylethylcarbinol [$(CH_3)_2$-$C(C_2H_5)OH$]. It occurs as a colorless, volatile, oily liquid, having an unpleasant ethereal odor and a burning, camphor-like taste. It is produced by the interaction of amylene, water, and sulphuric acid. Its specific gravity at ordinary temperatures is 0.820, and its boiling point is 99°-103° C. It is soluble in 8 parts of water and mixes freely with alcohol, ether, chloroform, and glycerin. It should be kept in well-stoppered bottles.

DOSE AND MODES OF ADMINISTRATION.—The dose of amylene hydrate taken by the mouth, for adults, is 30 to 90 minims (2 to 6 c.c.). If it is to be administered by the rectum, slightly larger amounts are required.

The disagreeable taste of amylene hydrate may be avoided by enclosing it in capsules (15 minims in each; 3 capsules at a dose) or by administering it in flavored solutions such as the following:—

℞ *Amylene hydrate*. 1 dr. (4 Gm.).
  Water .... 2 oz. (60 c.c.).
  Orange-flower
    water .... 2 oz. (60 c.c.).
  Syrup of bitter
    orange .... 1 oz. (30 c.c.).
M.
Of this one-half may be taken at night.

Where an analgesic effect is required in addition to the hypnotic influence, morphine may be combined with amylene hydrate, as in the following formula, recommended by Fisher:—

℞ *Amylene hydrate*. 1½ drs. (6 Gm.).
  Morphine hydro-
    chloride .... ¼ gr. (0.015 Gm.).
  Distilled water .. 3 oz. (90 c.c.).
  Extract of lic-
    orice .... 2½ drs. (10 Gm.).
M. Sig.: To be taken in two doses two hours apart.

Amylene hydrate may also be given in wine, beer, or brandy. A mixture of wine and syrup of licorice forms an especially good vehicle.

It cannot be employed subcutaneously, owing to the severe irritation and pain produced.

PHYSIOLOGICAL ACTION.—Amylene hydrate, like alcohol, causes a primary apparent excitement followed by depres-

sion and ultimate paralysis of the nerve-centers. The brain, cord, and medulla are stimulated and depressed in succession, the secondary results being sleep, abolition of reflex activity, and respiratory arrest. In the lower animals large doses have been found to induce cardiac depression and a pronounced fall in the body temperature. The latter effect has been credited to a direct action of the thermic centers. In man, however, amylene hydrate in moderate doses does not influence the temperature to any degree, even in fever. Neither does it depress to any marked extent, except in grossly excessive doses, the cardiovascular functions and respiration,—a feature in which it is superior to chloral hydrate. Amylene hydrate has but little influence on general metabolism. The elimination of urea is said to be more or less diminished after its internal use.

Locally, it is somewhat of an irritant. Upon subcutaneous injection tissue necrosis and abscess formation may result.

UNTOWARD EFFECTS; POISONING.—According to Scharschmidt, some patients perspire freely at the beginning of the effects of amylene hydrate. Occasionally excitement similar to that produced by alcohol or slight degree of stupor are produced by it. Headache and dizziness in a few instances follow its use.

Four cases of poisoning from overdoses were witnessed by Dietz. The symptoms consisted of deep sleep, from which the patients could not be aroused, complete motor paralysis, and loss of sensibility, including both touch and pain. The pupils were dilated, and reacted but slowly to light; the corneal reflex was abolished. Respiration was slow, superficial, and irregular; the pulse small, soft, and infrequent, and the temperature, in two instances, lowered to 95° F. Artificial respiration was required in one case. During recovery mental confusion and motor inco-ordination were conspicuous. In each case the overdose had been taken through neglect to shake the bottle in which the drug was mixed with syrup. Dietz advises that to avoid such accidents the drug be administered in capsules.

No instances of amylene-hydrate habit or cachexia have been observed (Flint).

THERAPEUTIC USES.—Amylene hydrate was introduced in medicine as a hypnotic by von Mehring, and has since held a favorable position as such, though, as Cushny states, it "has not received so wide a trial as it would seem to merit." Its effects rather closely resemble those of paraldehyde, but it leaves no bad taste in the mouth or disagreeable odor on the breath, such as are noticed with paraldehyde after the patient has awakened. In hypnotic power it is stronger than paraldehyde, but weaker than chloral hydrate. Likewise it is believed to exert a greater depressing influence on the heart than paraldehyde,—though less than chloral hydrate. Kirby and Griffith recommended that this drug be always used in heart disease in place of chloral. They also stated that in their experience amylene hydrate did not lose its efficiency upon continued use,—though given during three months in some cases,—and that the deep and refreshing sleep produced by the drug was praised by patients oftener than in the case of any other hypnotic.

Amylene hydrate differs in its action from chloral in that it does not increase nitrogenous wastes. According to Peiser the quantity of nitrogen eliminated by the urine after amylene hydrate is, in fact, lessened. This author therefore prefers the drug to chloral whenever the hypnotic effects are to be continued for a long time and in all affections associated with an exaggerated decomposition of albumins,—in fever, in anemia, pulmonary tuberculosis, and diabetes.

Sleep follows the ingestion of amylene hydrate much more promptly than after sulphonal, and it does not tend, as does the latter, to produce drowsiness and giddiness on the following day.

On the whole, amylene hydrate is, according to Kirby and Griffith, a reliable hypnotic if given in sufficient dose, though it is somewhat less certain in effect than chloral or morphine. When given by the rectum (in an enema with gum arabic and water), amylene hydrate brings on sleep in fifteen to forty-five minutes, or even sooner, though occasionally it fails entirely to do so.

Amylene hydrate acts satisfactorily in insomnia associated with **nervousness, ex-**

cessive **mental strain, fevers,** and **anemia.** Its usefulness in **cardiac states** has already been referred to.

In **gastric disorders** its oral use is apt to result in local irritation and nausea; in such cases it should be administered by the rectum. It is less irritating to the rectal mucous membrane than chloral hydrate.

In the insomnia of **mental diseases,** amylene hydrate has seen extensive service. In a series of 149 cases Lehmann obtained good results with it. In **mania** large doses were required. Cases of **paralysis of the insane** were benefited, but in the insomnia of **melancholia** it was less effective. It proved to be more efficacious and less unpleasant than paraldehyde.

Avellis found amylene hydrate generally effective in **alcoholic delirium.**

In a case of **opium addiction** in which chloral, bromides, paraldehyde and hyoscine, singly or variously combined, had given indifferent results, amylene hydrate produced sleep lasting through the night with but little or no intermission (Kirby and Griffith). Like results have been noted by other observers.

In **pulmonary disorders,** G. Mayer found amylene hydrate not only to produce sleep, but apparently to exert a decided sedative influence on the cough. In **tuberculosis** it sometimes proved useful in this respect after morphia had had but little effect. When there was pain or very troublesome cough, however, it was not uniformly successful.   S.

AMYLOFORM.—Amyloform is a

condensation product of formaldehyde and starch, first prepared by Classen, of Aachen, in 1896. It occurs in the form of very fine, white, odorless, and tasteless powder, which is insoluble in ordinary solvents. It remains undecomposed at a temperature of 180° C.

PHYSIOLOGICAL ACTION.—Amyloform is but slightly irritating. It is strongly antiseptic, disinfectant, deodorant, and absorbent, and is said to have all the advantages of iodoform without possessing its disagreeable odor. When applied to living tissue it is broken up into its two components,—formaldehyde and starch,—as shown by the fact that formaldehyde can be detected in the purulent discharge from suppurating wounds to which it has been applied (Classen). No symptoms of general intoxication are produced by the application of amyloform, though temporary smarting sensation locally is sometimes complained of. The secretions from open surfaces are rapidly checked by it.

THERAPEUTIC USES.—The drug is employed either as a dusting powder or in an ointment. Its uses are much the same as those of iodoform. Bongartz employed it with success in cases of **deep wounds with bone suppuration** and in **varicose ulcers** of the leg. Heddaeus laid stress on its rapid disinfecting action on **tuberculous lesions.** Its most important use, according to this author, is in the treatment of **superficial suppurative affections.** Lougard and Beauchamp used the drug in numerous cases of **phlegmon, abscess, furuncle,** etc., including **gynecologic affections.** Krabbel, who tested it both bacteriologically and clinically, came to the conclusion that amyloform was in no way inferior to iodoform as an antiseptic. C. L. Schleich, however, contends that it holds free starch, which smears up the wound and greatly hinders favorable action of the formaldehyde it contains.

Contrary to iodoform, amyloform can be sterilized in dry or moist heat without being decomposed. Because of this property, amyloform gauze affords some assurances of asepsis which are not found in the other antiseptic gauzes. An emulsion for preparing amyloform gauze is:—

℞ *Amyloform*.75 grs. to 2½ drs. (5-10 Gm.).
Glycerin ... 2½ drs. (10 Gm.).
Alcohol ....12½ drs. (50 Gm.).
Ether .....10 drs. (40 Gm.).
Ol. ricini .. 7½ mins. (0.5 Gm.).

The indications for amyloform are the same as for iodoform. (Presse méd., Sept. 15, 1900.)

Good results obtained with amyloform. The writers prefer it to the latter drugs in incised **abscesses, ulcers, wounds, burns,** and **purulent otorrhea.** Besides being harmless and free from any compromising odor, it remarkably hastens cicatrization. Cipriani (Monats. f. prakt. Dermat., Oct. 15, 1900).

Amyloform used in fresh and neglected **wounds, ulcers of the leg, excoriations, intertrigo, felons, carbuncles, osteomyelitis, tuberculous ulcerations,** etc. The pure powder usually employed. This occasions slight burning in sensitive patients, which, however, disappears soon. The chief features of its action are that it hastens granulation, diminishes secretion, and is, as a rule, non-irritating. Its freedom from odor and toxic effect is also noteworthy. A. Gerlach (Therap. Monats., Bd. xvi, Nu. 10, 1902).   S.

AMYL VALERATE (Amyl Valerianate).

—This is the isoamyl ester of isovaleric acid, and is a reaction product of amyl alcohol with sulphur and valeric acids. It represents the odoriferous principle of the apple, and occurs as a colorless liquid of specific gravity 0.858 and boiling point 190° C. (374° F.). It is insoluble in water, but dissolves in alcohol, ether, and chloroform. When in dilute solution, its ethereal apple-like odor is plainly evident.

PHYSIOLOGICAL ACTION.—Cider has long been believed by the laity to exert some favorable effect on calculous formations, and this seems to be borne out by the fact that amyl valerate actually does possess a certain solvent power with reference to cholesterin. Fifteen grains of cholesterin are dissolved by 70 grains of amyl valerate at 99° F., and by 46 grains at 104° F. Where the amount of cholesterin present exceeds the dissolving power of the valerate, it is, nevertheless, greatly softened,—to the consistency of gelatin.

The ingestion of amyl valerate induces primary general excitation and acceleration of the pulse, followed by somnolence (Pouchet). In addition to modifying or dissolving cholesterin, it tends to relax the bile-duct when in spasm.

THERAPEUTIC USES.—Amyl valerate was introduced by Blanc as an antispasmodic for use in **hepatic** and **renal colic,** and as a solvent for cholesterin calculi. It is said in hepatic colic not only to overcome the acute attack, but to prevent recurrences. No solvent effect on renal calculi is, however, claimed for it. The drug is administered in capsules; a capsule containing 2 to 6 minims (0.12 to 0.4 c.c.) may be given every half-hour, or one containing a somewhat larger amount, three times daily. The use of amyl valerate should be continued for some days after the acute disturbance has subsided.

Amyl valerate has also been employed in **muscular rheumatism,** in **dysmenorrhea,** and as a sedative in **hysteria.**   S.

ANALGEN

(quinalgen; labordin) is, chemically, the benzoylamido derivative of orthoethoxyquinoline $[C_9H_5.(OC_2H_5)-N.H.(CO.C_6H_5)N]$. It bears the same relation to quinoline as acetphenetidin does to benzene, with the exception that in analgen the benzoyl group takes the place of the acetyl in acetphenetidin. With the exception of thallin and thermifugin, it is the only member of the quinoline group of coal-tar analgesics or antipyretics which is still occasionally prescribed. It occurs in the form of colorless, tasteless crystals, soluble in hot alcohol and in acidulated water, slightly so in cold alcohol, and insoluble in pure water.

PHYSIOLOGICAL ACTION.—Analgen possesses the same antipyretic and analgesic properties as acetphenetidin, and its mode of action is closely similar (v. Acetphenetidin). With large doses, the same circulatory depressant tendency is present as with other coal-tar drugs. Analgen is more toxic than acetphenetidin, though less so than acetanilide. It is the least dangerous of the quinoline derivatives.

Analgen given experimentally to mammals induces motor depression and diminished reflex response, followed, with toxic doses, by cyanosis and convulsive movements.

The effects of analgen, when it is ingested, begin only after the benzoyl group in it has been set free by the gastric juice. Its action is, therefore, somewhat slower in appearing than is the case with acetanilide and antipyrin, and is to a certain extent inconstant.

A special feature of the action of analgen is that in large doses or upon continued use it produces a reddish discoloration of the urine. This coloration, when slight, is rendered more marked by the

addition of acetic acid (1 to 10). According to some, the coloration is due merely to the presence of decomposition products of analgen in the urine; according to Moncorvo, on the other hand, it is due to blood-coloring matter.

THERAPEUTIC USES.—The average dose of analgen for adults is 7½ grains (0.5 Gm.). According to Goliner, the maximum single dose is 15½ grains (1.0 Gm.) and the maximum daily amount 45 grains (3 Gm.). The drug has been used chiefly as an antineuralgic and antipyretic. Of late its use has, however, greatly diminished, the official drugs acetanilide, antipyrin, and acetphenetidin meeting with greater favor. Besides, the use of any antipyretic has justly lost favor.

Scholkow, Foy, Spiegelberg, and Maas found analgen effective in a large number of cases of **neuralgia.** According to Foy, who used it in 200 patients, the full dose of 15 grains (1.0 Gm.) was necessary to produce relief. In the pains of **tabes, zona,** and **hysteria,** the results were less brilliant, but in **acute articular rheumatism** and **muscular rheumatism** distinct benefit was noted in many instances. According to Maas, patients suffering from **pulmonary tuberculosis** experience "a peculiar feeling of wellbeing" from its use. Moncorvo used analgen in 59 children, 33 of them presenting various **malarial** manifestations, with satisfactory results. It was readily taken, because tasteless, and in no instance exerted any unfavorable action on the circulation or respiration. The urine became colored a deep yellow or red, but albumin and sugar were never detected. It acted satisfactorily as a sedative in **chorea,** hysteria, and **partial epilepsy** and was found useful to relieve **pain** of various kinds, including that of **Pott's disease** and **hip-joint tuberculosis.**

Occasional instances of untoward secondary effects are recorded by Scholkow and Spiegelberg, including headache, tinnitus, nausea, diarrhea, and tremor. Patients taking analgen should be informed of the red discoloration likely to appear in the urine, lest they be unduly frightened thereby.   S.

ANAPHYLAXIS.—This term was introduced by Richet of Paris in 1902 to designate a peculiar power possessed by certain poisons of increasing the sensitiveness of an organism to their toxic action. Von Pirquet, on the plea that it implied absence of systemic defense, whereas the reaction was one occurring beside, though linked to, immunity, termed it *allergy,* meaning another or additional reaction. Until the nature of the process is better known, however, it is preferable to employ Richet's original term, since what it does mean is a condition of hypersensitiveness which may ultimately prove to be but a phase of immunity.

Symptoms.—Diphtheria and tetanus antitoxin and other sera, antityphoid, antidysenteric, antiplague streptococcic, etc., give rise, as is well known, to untoward effects which formerly were attributed to "idiosyncrasy," "supersensitiveness," etc. The various phenomena developed have been called *serum disease* by von Pirquet, though the term applies specifically to one syndrome following occasionally injections of horse serum, the proteins of which is the harmful factor. While, for example, the use of diphtheria antitoxin is, as a rule, devoid of danger, such hypersensitive persons, often owing to previous injections, the presence of asthma, and sometimes without apparent cause, become seriously ill—fatally so in some rare instances.

The interval between an injection and the appearance of the morbid symptoms may be but a few minutes, several days, or even weeks. As a rule, however, it occurs before the eleventh day. A second injection is thought to be safe, where the first injection has given rise to no untoward effect, within six days, but this rule cannot be accepted as infallible. The attack may consist only in more or less redness of the face or severe urticarial eruption over the face and body, with intense pruritus; but, as a rule, it is far more severe, there being fever, with leucocytosis, usually eosinophilic, swelling of the lymphatic glands, edema, pains in the joints and in the back, albuminuria, a marked rise of blood-pressure, followed in severe cases by a decline of pressure—usually a precursor of death.

The suddenness with which lethal symptoms appear is sometimes appalling.

Thus some years ago E. L. Boone referred to "an apparently very strong and extremely well developed boy of 10 years who was given 4000 units of diphtheria antitoxin below the scapula. This was almost immediately followed by a loud cry of distress, strangling and choking cough, dyspnea, cyanosis, pallor about the lips, frothing at the mouth, a convulsion and death—all within 5 or 6 minutes." In another case, recorded by W. W. Hendricks, but 1000 units had been injected as a prophylactic, also in the scapular region, the child, a boy of 7 years, being perfectly well. "In 5 minutes," states the author, "the child was brought back unconscious . . . The skin was livid, the lips and nails blue, the lips and eyes swollen, the eyes half open, the pupils equally dilated, and the conjunctivæ injected. The jaws were firmly closed and a frothy mucous was found coming from the mouth and nose, the tongue was found swollen, and protruded when the jaws were forced open." These cases illustrate the fact that no evident disease may be present to warn the physician, and, moreover, that the smallness of the dose of diphtheria antitoxin may not prevent morbid effects.

Case of acute anaphylaxis in a young man following the administration of 10,000 units of antitoxin for diphtheria. In 5 minutes symptoms of respiratory distress began to develop and patient became very restless and apprehensive. The respiratory symptoms became progressively worse and patient more and more cyanotic until voluntary respiration ceased at 12.55 A.M. 10 minutes after the antitoxin was administered. Artificial respiration, oxygen and stimulants had not the slightest effect. The heart beat weakened and finally stopped at 1.10 A.M. It was subsequently ascertained that since he was a child cats caused attacks of sneezing whenever they came in his vicinity. He also was troubled with hay fever every fall until last fall, when he was on the Lakes and escaped his usual autumn attack. C. W. Carr (U. S. Naval Med. Bull., July, 1918).

As regards the development of untoward phenomena long after the initial treatment, Gillespie (Austral. Med. Gaz., June 22, 1912) records a case in which very serious symptoms were caused by the injection of antidiphtheritic serum about 18 months after a previous injection. The patient collapsed 15 minutes after the injection, became unconscious, vomited 5 times in 6 hours, had very shallow respiration, 35 to the minute, a pulse of very poor tension, 120, regular, and a temperature of 101.2° F. (38.4° C.). He began to recover consciousness at the end of 4 hours of active treatment, and made a good recovery, except that on the sixth day an urticaria developed.

Such cases are *extremely rare,* however, so rare in fact, that some observers of vast experience have never witnessed it. This fact should be borne in mind, for Guaita (Semana Medica, Aug. 21, 1913) relates a number of instances in which the parents refused to permit the use of antitoxin in diphtheria for fear of anaphylaxis, as the child had been injected with antitoxin on some previous occasion. In all his experience, and in that of Penna at the contagious disease hospital, Cabrera's at the diphtheria pavilion in the children's hospital and of others he cites, no instance of anaphylaxis has been encountered, although some of the patients had received several injections of antitoxin. He declares that this dread of anaphylaxis is irrational and extremely dangerous.

Cutaneous eruptions, however, are relatively common. Thus, Sturtevant (Archives of Int. Med., Jan., 1916) in a series of 500 cases found that out of 422 which had received but one injection, 20 per cent. had an urticarial or erythematous rash. The reaction occurred as a rule between the fifth and ninth day, though occasionally as early as the first and late as the nineteenth day, this being in no way influenced by the dose. Nausea and vomiting occurred in 9 per cent. of the reacting cases, and was more likely to occur and to be severe and prolonged if the dose of serum was increased. Albuminuria and edema appeared occasionally, and joint symptoms, sometimes severe, in about 14 per cent. of the reacting cases. When a given amount of serum was administered in 2 or more doses, it seemed as likely to produce a reaction as a single injection.

The large proportion of untoward effects in Sturtevant's cases does not seem to attend the use of foreign sera. This is well shown by F. Cuno's experience (Deut. med. Woch., May 14, 1914) in 3500 children. Of these, 97 received second injections at intervals of from 1 to 114 months after the first administration; 11 received both second and third courses of injections with intervals of from 1 to 130 months between the several courses; and 96 children had repeated doses from 10 to 63 days after the primary. This makes 207 in all who had second courses of injections, and of these only 1 showed symptoms of anaphylactic response.

Scarlet fever serum seems also to be less benign in its effects. Thus Nemmser (Deut. med. Woch., Apr. 17, 1913) observed no anaphylactic symptoms in 3000 children at the Petrograd Hospital for Infectious Diseases, after a single prophylactic injection. In 1002 recorded cases which had received 2 or more injections, however, serum eruptions were mentioned in 42 cases, *i.e.*, in less than ½ of 1 per cent., with no serious phenomena.

In **alimentary anaphylaxis** we have a form caused, as its name indicates, by certain foods, notably eggs, milk, and mussels. As described by Laroche, C. Richet, Jr., and F. Saint-Girons (Paris Méd., Apr. 18, 1914), the symptoms in severe cases may appear from 15 seconds to 45 minutes, and usually consist at first of urticaria, violent cramps, or vomiting. Diarrhea almost always follows, and respiratory and nervous disturbances may also appear. Mild alimentary anaphylaxis is much more frequent, and may occur either in adults with previous slight intolerance to some single article of food, or in children the variety of whose diet is increased too suddenly. Thus a child of 3 to 5 years may have taken 2 or 3 eggs a day for some weeks or months; gradually there appear disturbances such as chronic indigestion, heavy breath, constipation or diarrhea and urticaria, prurigo, or eczema. The urticaria sometimes recurs after each meal, at other times is practically chronic. At times edema of the face, eyelids, or limbs appears. Excessive feeding and insufficiency of the digestive secretions appear to favor alimentary anaphylaxis. Although the quantities of food, *e.g.*, of egg albumin, required to bring on symptoms need be only trifling, the amounts necessary to establish the anaphylactic state are usually relatively large, at least 1 or 2 eggs daily in addition to the ordinary diet. Diagnostic features are the suddenness of symptoms, almost immediately after ingestion, and the fact that symptoms appear each time an attempt is made to accustom the subject to the food in question, no matter how small the quantity.

> The writer observed that in cases of intolerance of eggs, shellfish, etc., the symptoms took the form of circumscribed transient edema, urticaria, migraine, or asthma. In such cases a small amount of the harmful food taken an hour before the meal, or a tablet of 0.4 or 0.5 Gm. (6 or 7½ grains) of **peptone**, gives good results. The peptone seems to be polyvalent for most of the articles causing the anaphylaxis. Some patients require the continuous use of the peptone, others do better when it is given for 3 to 8 days followed by an interval of the same length. With this simple measure they have succeeded in curing the tendency in time in many cases. Pagniez and Valléry-Radot (Annales de Méd., Oct., 1920).

Anaphylaxis is thought to explain *various diseases of childhood.* Thus Pisek and Pease (Boston Med. and Surg. Jour., Jan. 25, 1912) hold that among these are many spasmodic conditions in children which have long been attributed to exaggerated irregularity of the children's system. The suddenness of their onset and the rapidity with which they disappear suggest that they belong to the group of anaphylactic reactions—laryngeal spasm, tetany, eclampsia, certain forms of asthma, and some of the severer types of convulsive seizures, for example.

Among the diseases also attributed to anaphylaxis are *hay fever.* The newer literature upon this subject is given under Hyperesthetic Rhinitis, in this volume.

Diagnosis and Pathogenesis.—The symptoms of anaphylaxis include, we have seen, several pointing to involvement of the respiratory, vascular, cutaneous, and gas-

tro-intestinal systems. The dyspnea and in severe cases apnea, and the resulting cyanosis have been found by Biedl and Kraus, Anderson and others, to be due to spasmodic contraction of the bronchial musculature—the identical causative feature of bronchial asthma. *Where asthma exists,* therefore, *anaphylaxis is likely to occur.* This symptom may appear not only in serum disease but sometimes in alimentary anaphylaxis as well, as shown by Talbot (Boston Med. and Surg. Jour., p. 708, 1914, and 191, 1916) Schloss (Am. Jour. of Dis. of Children, p. 346, 1916) and others, the vomiting, abdominal pain and diarrhea being but eliminatory phenomena.

The peripheral symptoms, cutaneous and vascular, are seemingly closely related, not only mutually, but also with the respiratory signs. The toxemia which in the lungs produced spasm of the bronchial musculature, likewise provokes spasm of the vascular muscles; hence the angioneurotic edema, of which the swelling of the lips, tongue, buccal mucosa, pharynx and esophagus are corresponding expressions. A similar constriction of the pupillary vessels causes the bilateral dilatation of the pupils. Far more dangerous in its effects, is the simultaneous contraction of the cardiac vessels among others and ischemia of the myocardium as result, the blood-pressure being at first high, then increasingly low, until prostration, collapse and death supervene, all in rapid succession. The urticaria, urticarial wheals, erythema and eczema are also the result of vascular spasm, their immediate cause being imprisoned wastes—ephemeral in some cases, persistent and grave in others.

[This interpretation of the pathogenesis of anaphylaxis summarizes personal studies of the subject. As we shall see below we are dealing from my viewpoint, with a vasomotor spasm, due undoubtedly to intermediate protein wastes—whether derived from horse serum, ingested foods or parenterally introduced proteins. Gay and Southard, Auer and Lewis, and others several years ago found that the asphyxia was due to tetanic contraction of the finer bronchioles, with alternating rise and fall of the blood-pressure. C. E. DE M. S.]

Various **tests** have been proposed to determine the identity of the protein to which a given subject may be sensitive—where undetermined foods provoke toxic phenomena.

The simplest of these is the *elimination test,* which consists in placing the patient on a bland diet known to produce no untoward effects, then adding thereto a suspected article of diet at a time at 3 or 4 days' intervals until the characteristic morbid effects are noted.

The *cutaneous test* is more satisfactory. The skin is abraded without drawing blood and an aqueous 5 per cent. solution of the suspected food or of pure proteins is rubbed in as in ordinary vaccination, controlling it by means of a 5 per cent. lactose in normal saline solution. An urticarial wheal with a pink areola appears in about 10 minutes and persists about 30 to 40 minutes.

The *intracutaneous test* (not *subcutaneous*) is still more sensitive, but somewhat painful. A small drop of a 2 per cent. aqueous solution of pure protein is injected *into* the skin (not under it, as alarming symptoms might result) with a very fine needle, the syringe being laid almost flat on the arm. The same urticarial wheal with an erythematous areola, with, perhaps, a small papule, develops in about 24 hours provided the reaction is positive.

Etiology and Pathology.—All proteins, living or dead, contain a poisonous substance which, under normal conditions, is destroyed in the gastro-intestinal canal in the course of digestion, during which the proteins are converted into the non-poisonous amino-acids. When, however, proteins, sera, eggs, milk, protozoa, bacteria, etc., are introduced otherwise than by way of the stomach and enteric canal, *i.e.,* parenterally, through the skin, the vessels, and perhaps the respiratory mucosa, wounds, etc., their toxicity is not eliminated, and it evokes, as antigen, a defensive reaction. The anaphylactic symptoms occur, however, when, after a first dose, generally termed the "sensitizing dose" of any kind of protein, is followed sometime later by a second dose— the "toxogenic dose." How are the morbid phenomena described brought about?

Many theories have been vouchsafed, but none so far have fully met all the phases of the problem. Richet thought the first dose caused the formation of "toxogenin" which, when the second dose was injected combined with the latter to form "apotoxin," the anaphylactic poison. While this earliest of the many theories proposed, including those of Gay and Southard, Besredka, and Vaughan and Wheeler, each of which supplied some elucidative feature, it formed the basis of Friedberger's second theory, which seems, at least, to account for most of the known facts. The first dose, he found, formed a toxic under the influence of the immune body increasingly developed by the animal after that dose. While this first poison is insufficiently active to awaken morbid phenomena, it increases greatly in quantity and virulence when the "toxogenic dose" is injected and becomes, together with the complement normally contained in the blood, the "anaphylatoxin" which causes the anaphylactic attack.

[While this theory best explains the formation of the anaphylactic poison, it does not explain the *manner* in which the poison produces *its effects*. This brings us back to the personal view that we are dealing with *an intense spasm of the vascular, cardiac and bronchial vessels* caused directly by the anaphylatoxin; upon this our therapeutic measures should be concentrated.—C. E. DE M. S.]

The many different procedures which have proved useful in preventing anaphylactic shock either prevent flaking of the blood serum or cause vasodilation. This indicates that anaphylactic shock is due to physical changes in the blood serum which permit flocculation of the molecules. The flakes thus formed obstruct the capillary network, and thus induce fulminating asphyxia. Prophylaxis and treatment call for measures to diminish the surface tension of the blood serum (**saponin, soaps, bile salts, anesthetics, hypnotics, lecithin,** etc.), or to render the serum more viscous (**sugars, glycerin, acacia, carbonates, alkalies,** etc.), or to dilate the blood-vessels to allow the passage of the flaked micella (**calcium,** lactate, atropine, etc.). Kopaczewski (Annales de Méd., Oct., 1920).

Emphasis laid upon anaphylaxis as a sequence of emaciation. In the infant with chronic anaphylaxis the emaciation may, of course, be attributed to gastroenteric indigestion, but the failure of digestion and assimilation may itself be explained as a consequence of the anaphylaxis. **Pepsin** and **pancreatin** are both indicated to place the *primæ viæ* in favorable condition. The principal therapeutic resource is injection of **boiled milk** subcutaneously to desensitize the patient. The use of **peptone** in urticaria and even for drug anaphylaxis has given some surprising results. Laroche, Richet, Jr., and Saint-Girons (Bull. méd., July 10, 1920).

Prophylaxis.—Various measures have been proposed, but, of all, the most satisfactory, when *diphtheria antitoxin* is to be used, is that advocated by William H. Park in 1912 (Med. Record, Nov. 22, 1913). Experimentally, he found that a single does of antitoxin given after infection would save animals when the same and even larger amounts given in divided doses would utterly fail. Cases of diphtheria were treated with one massive subcutaneous injection of antitoxin in which the antitoxin content of the blood was tested from hour to hour. It was found to increase in all cases for the first 3 days. The apparent improvement following a second dose of antitoxin was shown to be due, partly to the continued absorption of the first injection, and partly to the necessary time required for recovery of the local process. When the first injection was of fair size, a second added no real effect. During 1912-1913, over 95 per cent. of all cases of diphtheria treated at the Willard Parker Hospital received but 1 injection of antitoxin. The mortality was the lowest in the history of the hospital. The usual amount given was 5000 units in the milder cases, 10,000 units in the moderate or rather severe cases, and 20,000 units in the malignant cases. In the latter, the antitoxin was given intravenously whenever possible. The same number of units given intravenously was fully fourfold the value of the same

amount given subcutaneously. Intramuscular injections had the advantage over subcutaneous, in the rapidity of absorption, but when fairly large amounts were given, it was difficult to insure that the antitoxin remains within the muscle. As a rule cases not requiring intravenous injections could be treated by either the subcutaneous or intramuscular methods.

Concerning the danger of anaphylaxis from *primary subcutaneous injections,* the same author submits the results obtained by the New York Health Department. Over 30,000 cases of *diphtheria* had been treated with antitoxin since 1895 in the contagious disease hospitals. There had been no fatal cases of anaphylaxis and only one in which dangerous symptoms developed. In over 100,000 persons injected outside of the hospitals, there had been but 2 fatal cases, in 1 of which marked *status lymphaticus* existed. In a great many children in the *scarlet fever* service, a primary immunization injection of diphtheria antitoxin had been followed by a second larger subcutaneous injection at a period at which anaphylaxis should be marked. In no case had any dangerous symptoms developed. *Unless, therefore, there was a history of asthma,* there seemed no reason to avoid the giving of a primary serum injection on account of fear of later having to give another injection, either in the near future, or after a number of years.

[The words "status lymphaticus" and "asthma" are italicized because I consider the thymus as a leading malefactor in the lethal process. In a series of articles on this organ (New York Med. Jour., March 6, 1915 to Feb. 5, 1916 inclusive) I urged that under the influence of excessive feeding its sponge-like tissues became greatly engorged, in part by cellular elements. Since then Lesné and Dreyfus found that anaphylactic death could be prevented in highly sensitized animals by starving them 4 or 5 days before the toxogenic dose was administered. Again, as we shall see elsewhere, thymic death may occur during swimming, dancing, coitus, etc. From my viewpoint this is the result of a temporary rise of blood-pressure which causes sufficient congestion of an enlarged thymus to cause asphyxia by compressing

the trachea—a factor which should be borne in mind in the present connection. Asthma and status lymphaticus are important danger signals; but they are not always present, even though the thymus be greatly enlarged. The diagnostic signs of enlargement are described in the article on the THYMUS in vol. viii.—C. E. DE M. S.]

Besredka, who has done some of the best work available on the subject, states that anaphylactic shock may be largely averted by **heating the serum to 56° C.,** or by giving normal serum **per rectum** before giving the subcutaneous dose, or, again, by giving a **small subcutaneous dose** before the larger dose. Vaughan, Jr. (Amer. Jour. Med. Sci., Feb., 1913) states that a preliminary dose of as little as 0.1 or 0.2 c.c. (1½ to 3 minims) suffices, the therapeutic dose being given a couple of hours later if no untoward effects follow the test dose. This measure does not always protect. Thus Koch (Berl. klin. Woch., June 28, 1915) reported the sudden death of a child of 6, with scarlet fever and diphtheria, at once after injection of antistreptococcus serum, after a preliminary small injection. The child had been injected with diphtheria antitoxin the third and sixth days of his illness, and the intravenous antistreptococcus serum injection was given the twentieth day. Nothing could be found to explain the sudden fatality but anaphylactic shock, except that the child was debilitated, its resisting powers at a low ebb. In such cases serotherapy should be applied with special caution.

[We have seen under "tests" that even the *sub*cutaneous test doses may evoke grave symptoms, and even death. We can ascertain the susceptibility of the patient by the *intra*cutaneous test without exposing the patient.—C. E. DE M. S.]

S. Wyard (Lancet, Jan. 20, 1917) states that by the injection of a subminimal dose the individual is thereafter rendered refractory for a time, during which further and even larger doses may be safely given. In man sensitization rarely, if ever, reaches such intensity as to cause reaction with 1 c.c. (16 minims) of blood-serum, so that in the use of diphtheria or tetanus antitoxin, if it be considered unsafe to inject a large dose at once, 0.5 to

1.0 c.c. (8 to 16 minims) may be used as a preliminary injection, followed 5 or 6 hours later by any further dose that may be considered necessary. Should even greater rapidity be desirable, such a preliminary dose may be followed in 5 or 10 minutes by a larger, and every 5 minutes or so afterward by steadily increasing amounts, whereby in a very short time enormous doses may be given, and without risk of anaphylactic shock. In the case of *tetanus antitoxin* where prophylactic doses were given, these were practically all innocuous.

The amount of serum actually employed varies from 3 to 5 c.c. (48 to 81 minims), according to the concentration of the sample. An interval of anything up to 5 weeks between two such doses will never, according to the author, give rise to symptoms. About the sixth week, however, hypersensitiveness may appear.

In 3 cases of alimentary anaphylaxis antianaphylaxis treatment proved effectual. Two were in children who developed urticaria after eating eggs, or certain other food. The third was a young man with attacks of asthma nearly every evening, 3 or 4 hours after eating. All seemed to be cured completely by taking 0.5 Gm. (7½ grains) of **peptone** ½ hour before breakfast and dinner for 20 days, with appropriate dietetic restrictions. Joltrain (Bull. de la Soc. Méd. des Hôp., June 6, 1919).

Agreeing with the view that anaphylactic manifestations are due to the formation in the blood plasma, at the time of the second injection, of a colloidal flocculent precipitate which causes asphyxia by obstructing the capillaries, the writers tried various substances which might prevent it. Among the few compounds found effectual, **sodium hyposulphite** was by far the least toxic. Control animals, unprotected by this salt, invariably succumbed. Similar experiments with antidiphtheritic serum gave the same results. They deem addition of sodium hyposulphite in suitable amounts to therapeutic serums a simple, practical and harmless means of obviating anaphylactic phe-

nomena. Lumière and Chevrotier (Presse méd., Nov. 6, 1920).

The anaphylactic shock or *colloido-clasie sérique* can be warded off by intravenous injection of 0.5 to 2 Gm. (7½ to 30 grains) of **sodium carbonate** in 40 to 60 c.c. (1-⅓ to 2 ounces) of saline or distilled water. **Sodium bicarbonate** by the mouth, 10 to 15 Gm. (2½ to 3¾ drams) 15 minutes beforehand, will ward off the anaphylactic shock to a less extent. Sicard and Paraf (Bull. de la Soc. Méd. des Hôp., Jan. 28, 1921).

Treatment of Anaphylactic Reaction.— The term "anaphylactic shock" is occasionally employed in this connection, but is misleading, since an approach to true shock is only witnessed when the patient is virtually moribund, *i.e.,* when his blood-pressure has fallen below normal.

Anderson and Schultz found some years ago (1910), using highly sensitive guinea-pigs, that **atropine sulphate, chloral hydrate, plus urethane and adrenalin,** pure **oxygen,** both alone or **with chloral hydrate and adrenalin,** almost invariably prolonged life, but that it did not prevent their eventual death from low blood-pressure, though not from acute asphyxia. Rosenau and Anderson tried, besides these agents, ether, recommended by Besredka, **paraldehyde** and **magnesium sulphate,** but concluded that they had no influence on the outcome. Of these, **atropine, adrenalin,** intramuscularly or intravenously, **chloral hydrate, ether** and **pure oxygen inhalations,** and **artificial respiration,** might prove of service. A threatening case of anaphylaxis following the secondary use of cholera vaccine was successfully treated with **adrenalin** by Parhon and Bazgan (Bull. de la Soc. de Jassy, Jan.-Apr., 1916).

W. M. Crofton (Lancet, Jan. 20, 1917) found that 1 c.c. (16 minims) of **pituitrin** given at once relieves the collapse and spasm of the bronchioles within a few minutes. The dose is repeated if the symptoms show any signs of returning.

Edema of the larynx was evidently present in a case reported by M. B. Arnold (Lancet, Jan. 27, 1917), in which **tracheotomy** relieved all the respiratory phenomena and the cyanosis.

[The main features of the morbid

process seem to me to have been overlooked. That an intoxication prevails is undeniable. Enhancing the osmotic properties of the blood and its viscosity, **intravenous saline solution infusions,** preceded perhaps by **bleeding,** is the rational measure indicated. If the blood-pressure is low, as it is late, *i.e.,* during the second stage, **adrenalin** should be added, the 1:1000 solution being injected drop by drop with a hypodermic syringe into the rubber tube of the irrigating instrument. Intramuscular injections of **pituitrin** may also be used.—C. E. DE M. S.]

ANEMIA, PERNICIOUS PROGRESSIVE. — DEFINITION. — A

form of anemia characterized by a progressive destruction of the red corpuscles which points to a fatal issue.

SYMPTOMATOLOGY.—Pernicious anemia develops insidiously, though an abrupt onset occasionally occurs, especially in pregnant or puerperal women. The most evident symptom is pallor of the face and body, which gradually becomes extreme and assumes a lemon-yellow tint. This yellowish color deepens as the case progresses; it may appear suddenly, but in the majority of cases it develops gradually, following the insidious course of the disease. The mucosæ are similarly affected.

There is great weakness with all its attending symptoms: inordinate palpitations and dyspnea on exertion, sighing, and slow delivery in speaking. The pulse, which may be strong at first, is regular, but rapid, soft, and compressible, in the majority of cases, more or less fever being usually present. The temperature is extremely irregular. Slight evening pyrexia is seldom absent in advanced cases.

Cardiac murmurs, especially of the hemic type, are usually to be heard, especially at the base, and signs of

fatty degeneration may be detected by auscultation, although there is usually no arterial degeneration or valvular disease. A loud venous hum can sometimes be detected in the vessels of the neck, the so-called *bruit de diable* with exaggerated cardiac impulse. Edema of the ankles, face, and lungs and dropsical effusions may appear at any stage.

There may be hemorrhages into the mucous membranes, epistaxis, menorrhagia, and purpuric eruptions in ad-
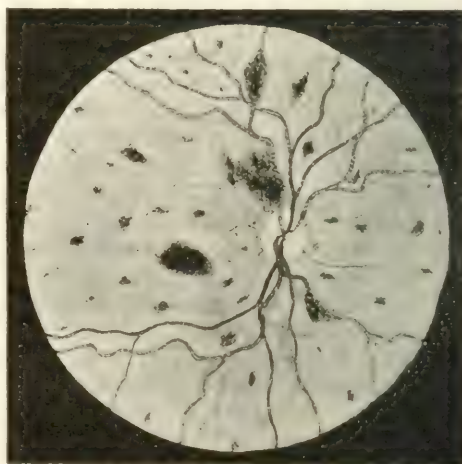
Fundus oculi in a case of pernicious anemia, showing retinal hemorrhages. (*Bramwell.*)

vanced cases. Ecchymoses in the skin and mucous membranes are sometimes noticeable in advanced cases. Retinal hemorrhages may occur.

A study of 148 cases led the writer to conclude that while pernicious anemia has its own characteristic diagnostic findings, these may be simulated closely by anemias resulting from various diseases, particularly in those due to some definite septic, toxic or malignant condition. The diagnosis should rest, not on the blood findings alone nor on the blood findings and symptomatology, but on both of these features in the absence of any discoverable cause for the ane-

mia. The disease is more common in males and is most frequent in the fourth and fifth decades of life. The cardiac symptoms and physical findings are among the most common symptoms. These findings are the result of myocardial weakness and relative insufficiency.

The systolic pressure is almost never above normal, but tends to be below the lower limit of normal; the diastolic pressure is disproportionately low and the pulse pressure high. The urine is usually of a fairly low specific gravity, rather increased in quantity, and rarely contains albumin. Albumin with casts means nephritis, which may be the cause of the anemia rather than the effect. Pernicious anemia is characterized by an irregular temperature, which is not often above 101°; there are often recessions to normal of variable duration. Achylia gastrica is so much the rule that the presence of free hydrochloric acid may raise a doubt as to the diagnosis. The gradual decrease in the leucocyte count, especially in the relative and absolute number of polymorphonuclears, is of serious prognostic import. The diagnosis of pernicious anemia should be made with the utmost reserve in the presence of a leucocytosis. J. G. Carr (Amer. Jour. Med. Sci., Nov., 1920).

Gastric and intestinal disorders are the rule, although the general nutrition is apparently preserved, the appetite being sometimes voracious, and the patient becoming obese. Nausea is frequently an early symptom. Dyspepsia, vomiting, and diarrhea usually prevail, though some cases suffer from constipation. The gastric region is tender to pressure, and the tongue is pale and smooth. Eructations and anorexia are common. Involvement of the osseous system is occasionally indicated by sensitiveness of the bones, especially those of the sternum.

The familiar fact that this chronic disease ends in death in practically every case has rightly been attributed to the tardiness with which its true identity is recognized. So advanced have the lesions then become that remedial measures are of no avail. Efforts have been made, therefore, to discover initial symptoms. Schaumann (Deut. med. Woch., June 27, 1912) emphasizes the importance of a sign first pointed out by William Hunter: *soreness of the tongue and mouth,* and in some cases of the *throat,* the organ remaining moist and uncoated, though *deeply grooved.* These signs appear before the blood gives any positive indication of the nature of the disease. Zabel (Klin-therap. Woch., Jan. 6, 1913), who describes the lingual pain as *burning,* states that he has witnessed it in the simpler secondary anemias, but that it disappears in these disorders when the general condition improves. H. Stern (Deut. med. Woch., July 23, 1914) considers it the most reliable of the inaugural symptoms of true pernicious anemia.

In 4 cases of the classic type, Roccavilla (Policlinico, Sept., Med. Sec., 1916) noted *burning heat* and *dryness of the lips, tongue* and *throat* as the first sign of trouble. The complexion assumed a lemon yellow tint with greenish reflection in all but one of the patients.

An authoritative clinician, Friedenwald (Boston Med. and Surg. Jour., Aug. 1, 1912) noted that in a series of 58 cases all showed *gastro-intestinal symptoms.* There were loss of appetite, nausea, vomiting, indigestion (fullness, pressure, distention), diarrhea and constipation. Achylia gastrica was present in about 70 per cent. of the cases and even in the stage of apparent recovery the gastric secretion did not return.

Another feature in the early diagnosis of pernicious anemia worthy of closer observation in the future is the occasional early predominance of nervous phenomena. Thus, in several cases seen by C. E. Riggs (New York Med. Jour., July 15, 1913) *mental symptoms* recalling those of dementia paralytica and *spinal symptoms* resembling those of ataxic paraplegia had long preceded any of the blood characteristics. Wilson (Jour. Amer. Med. Assoc., Sept. 7, 1912) holds that if the spinal involvement, which, in a case of his own

consisted of degenerative vacuolization of the nerve-cells and replacement gliosis, were borne in mind, many cases that fail to be promptly recognized would clear up at once. The history of his case and the microscopic findings suggested the intestinal origin of both the pernicious anemia and the spinal disorder. On the whole, given a case in which *yellowish pallor* and *lassitude* are attended with *oro-gastro-intestinal phenomena* with *remission* and *periodical gastralgia*, a tentative diagnosis of the form of pernicious anemia most frequently encountered is warranted, even before the blood affords any clue to the identity of the disease. C. E. DE M. S.]

The respiration is usually accelerated, and dyspnea, air-hunger, and oppression in the chest are frequent symptoms. Pericardial and pleural effusions are sometimes observed.

Drowsiness is present in the majority of cases, but insomnia is occasionally noted. The patient is readily fatigued and even exhausted on the least exertion. The weakness increases until attacks of faintness supervene. The patient ultimately becomes bedridden.

Headache, vertigo, tinnitus, apoplectiform attacks, delirium, and other disorders of the nervous system, such as paresthesia, neuralgia, and extensive paralyses, have been noted. Mental torpor, somnolence, peevishness, confusion, delirium, and various psychic phenomena may also occur.

Absence of the knee-jerk is frequent, and is indicative of degeneration of the posterior columns of the cord.

The presence of grave pernicious anemia is to be suspected when *pulsation of the inferior vena cava* is discernible. It is best recognized by simple inspection, especially in the median line below the umbilicus, somewhat more to the left than to the right, and is visible as a double, undulatory rise of the surface in each cardiac cycle. Palpation is negative, and the pulsations disappear when the patient rises from the recumbent to the sitting or standing posture. L. Bard (Semaine méd., Mar. 25, 1914).

Jaundice is occasionally met with. The urine is dark and highly colored; it is of low specific gravity, and shows an increase of urea and uric acid and pathological urobilin. Indican may also be detected.

When the end is approaching, the temperature, which in the course of the disease is apt to rise toward evening, sometimes reaching as high as 102° F. (38.8° C.), recedes markedly, and the patient enters into a torpid condition ending in coma.

BLOOD EXAMINATION.—Before describing all the characteristics of the blood, a summary of its morbid changes may prove useful. Though sometimes dark and watery, the blood is, as a rule, pale. The red corpuscles are greatly reduced, sometimes as low as 143,000, though, as a rule, they do not go below 500,000. The percentage of hemoglobin is also greatly reduced, but not in proportion with that of the red corpuscles. The latter also show considerable alteration in size and shape. Some are large and ovoid (megalocytes); others are small, round, and dark red (microcytes), while others again are very irregular in shape (poikilocytes). Nucleated red cells, both normoblasts (normal in size) and megaloblasts (when very large), are a marked characteristic of the disease, while blood-plaques are either absent or present in very small number. The leucocytes, though relatively increased in respect to the red corpuscles, are usually normal in number, with the smaller mononuclear forms predominating.

In the pernicious anemia complicating pregnancy the blood findings

in the mother are characteristic. The red cells are decreased in number, even to 250,000. The blood does not show a proportionate decrease in its hemoglobin content, but there is a marked alteration in the shape, size, and staining of the individual cells. Macrocytes and microcytes abound and megaloblasts are occasionally present. Nucleated red cells do not as a rule appear until the disease is well advanced; they tend to appear in showers, and in some cases fail to appear or at least are not found even in the last stages of the disease. Poikilocytosis is marked; fibrin and blood platelets are diminished and the leucocytes are lessened in number. Palmer Findley (Trans. Amer. Gynec. Assoc.; N. Y. Med. Jour., Aug. 24, 1918).

To understand these blood changes, however, they must be analyzed from the standpoint of their cause. The two prevailing theories as to the pathogenesis of pernicious anemia are: 1. That the disease is due to breaking up of the blood-corpuscles (hemolysis). 2. That, owing to some defect in the blood-making (hemogenesis), the blood becomes vulnerable to the destructive influence of micro-organisms. At the present time the former view strongly prevails, the hemolysis, as urged by Grawitz, Hunter, Stengel, and others, being ascribed in great part to poisons absorbed from the alimentary canal, the disease being thus an autointoxication. The toxics, according to Sajous, promote and sustain hemolysis by causing an overproduction of antibodies, which not only destroy the pathogenic poisons, but also the red corpuscles. The hemosiderin found in the urine is the product of the broken down hemoglobin *i.e.*, the iron freed of hematin.

The writer regards hemosiderin granules in the urine as an aid to the diagnosis of both pernicious anemia and hemochromatosis. In a soldier of 46 years, showing hemochroma-

tosis, the diagnosis between this condition and syphilis became doubtful. There was enlargement of the liver and spleen and a peculiar gray pigmentation of the skin, and the urine was found to contain considerable hemosiderin granules. The patient died within 3 months with characteristic signs of hemochromatosis. The writer urged that hemosiderin granules are also found in the urine in eight-tenths of the cases of pernicious anemia, provided fresh urine be used for the test. P. Rous (Trans. Assoc. Amer. Phys.; N. Y. Med. Jour., Aug. 31, 1918).

While the presence of hemosiderin granules does not explain the etiology of hemochromatosis, it tends to account for its pathology, which perhaps is the result of interstitial inflammation of the pancreas, while the cirrhosis of the liver is probably secondary to accumulation of iron pigment in the cells. E. I. Opie (Trans. Assoc. Amer. Phys.; N. Y. Med. Jour., Aug. 31, 1918).

In a patient of 67 years, with chronic jaundice, the writer found in the spleen and liver a hemosiderosis comparable with that shown by Rous, but there was no cirrhosis of the liver. W. Tileston (Trans. Assoc. Amer. Phys.; N. Y. Med. Jour., Aug. 31, 1918).

Deficiency of red corpuscles (oligocythemia) is always very great; the blood is, therefore, pale and thin, resembling sherry wine. The oligocythemia is sometimes so marked that the normal proportion of 5,000,000 red corpuscles to the cubic centimeter is reduced to one-twenty-fifth of that number. Quincke reported a case in which, as previously stated, there were only 143,000 to the cubic centimeter immediately before death. This is an important diagnostic feature. There is no disease, except pernicious anemia, in which the number of red corpuscles is at any time reduced below 20 per cent. This affords a distinction between

pernicious anemia and latent gastric cancer, a disease with which the former is most likely to be confounded.

The hemoglobin is also greatly reduced (oligochromemia), but not in proportion with the cell reduction. The hemoglobin percentage was greater by 10 per cent. in a case seen by Osler. The relatively high percentage of hemoglobin depends upon increased average size of the corpuscles and in some cases on the presence of an unusual number of highly colored and minute microcytes. It also depends, in a measure, upon the time at which the examination is made. The icteric color of the skin and the dark urine are caused by dissolution of the red blood-corpuscles, and the hemoglobin estimated at one of these periods will thus be higher, owing to the more highly colored plasma. The red blood-corpuscles show marked signs of reversion to the type of blood which is normal in the cold-blooded animals.

There is also a species of degeneration closely resembling coagulation necrosis, and an alteration of the corpuscles, characterized by the appearance in their interior of certain corpuscles composed of modified hemoglobin— *dégénération hémoglobinémique.*

The process of regeneration is manifested by the presence of nucleated red corpuscles, which are divided by Ehrlich into two varieties: the normoblasts and the megaloblasts, the former corresponding to the hematinic evolution of adults, the latter to that of the embryo. The nucleus of the normoblast is extruded to form a new red corpuscle, while the nucleus of the megaloblast is absorbed. Fresh blood shows nucleated red corpuscles of large size, the megalocytes and gigantocytes previously mentioned.

Fürbringer has shown that a case is to be considered as one of true pernicious anemia only when one-fourth of the red corpuscles are macrocytes. The presence of megaloblasts is a sign that certain pathological changes are taking place in the red marrow rather than a distinctive feature of pernicious anemia. The macrocytes are more characterisic of pernicious anemia, because they are the direct precursors of the large red-marrow cells.

Misshapen corpuscles (poikilocytes) are very frequently observed, oftener, indeed, than in any other affection. Many small, imperfectly developed corpuscles (microcytes) are generally found.

In marked cases corpuscles endowed with motion are occasionally observed. According to Hayem, the red blood-corpuscles of normal blood are motionless. Conversely, the elements observed in cases of high degree of anemia are endowed with four kinds of motion: 1. A movement of the entire mass of the corpuscle. 2. The projection of mobile prolongations. 3. A movement of oscillation, manifested slowly by minute corpuscles. 4. A movement which results in changing the position of the corpuscles. These movable corpuscles are bodies arrested in their evolution and still retaining the contractile properties of the hematoblasts from which the red corpuscles originate. On superficial examination they might readily be mistaken for parasites.

Many years ago I observed distinct movements in the red corpuscles in a case of pernicious anemia, but made no public mention of the interesting fact. Senator has also called attention to the presence of small, mobile bodies observed staining the same as red corpuscles and resembling fragments of

hematin, thought to possess pathogno-
monic value.

PATHOLOGY.—In cases in which
the urine is dark the latter is found to
contain pathological urobilin: a sub-
stance known to be derived from the
disintegration of hemoglobin, and
which, according to Hunter, is of high
diagnostic significance. A peculiarity
of this highly colored urine is that it
presents a low specific gravity, averag-
ing 1.014. Occasionally, however, the
urine is habitually pale. The kidneys
are often the seat of fatty infiltration,
accompanied sometimes by thickening
of the interstitial tissue. Urinary reten-
tion, owing to the absorption of hemo-
lysins, whether of renal or cystic origin
—the latter in cases of enlarged pros-
tate for instance—may also act as cause.

> After a study of 14 cases the
> writer concluded that in a severe
> case the *renal function* is *disturbed*
> much as it is in advanced chronic
> nephritis. The disorder of excretion
> seems to be either a nutritional or a
> toxic disturbance in renal cellular
> activity. There is no other evidence
> of chronic nephritis in these cases,
> and the disturbance decreases with
> improvement in the anemia, unless
> the latter has been permanently dis-
> turbed. H. A. Christian (Arch. of
> Internal Med., Oct., 1916).

The gastric and intestinal disorders
are probably due to the formation of
poisons, which, we have seen, act, in
turn, as the etiological factors of the
general disease. The gastric and in-
testinal walls are often found to be the
seat of fatty change, and atrophied.
Intestinal entozoa underlie many cases.

> With the aid of the Abderhalden
> reaction the writer reached the con-
> clusion that there exists a definite
> causal relation between pernicious
> anemia and gastrointestinal disturb-
> ances. This suggests that autointoxi-
> cation of gastrointestinal origin is

an important pathogenic factor in
the process. Kabanoff (Roussky
Vratch, Sept. 7, 1913).

> A study of the chemistry of per-
> nicious anemia showed that it may
> be considered as the result of a gas-
> trointestinal disturbance leading to
> destruction of mucosa sufficient either
> to allow undigested proteins to leak
> through into the blood stream,
> where their partial digestion liberates
> protein poisons, or to the absorption
> of known hemolytic toxins produced
> in the course of intestinal putrefac-
> tion, such as, *e.g.,* p-oxyphenylethy-
> lamin. In either case, the poison has
> a destructive influence on the intes-
> tinal mucosa, as well as the more evi-
> dent hemolytic effect, and this re-
> sults in the establishment of a vicious
> circle. Sqeier (Jour. Lab. and Clin.
> Med., May, 1917).

Pernicious anemia may be due to an
infection of the intestinal tract with
the *Bacillus aërogenes capsulatus.* Her-
ter found this organism regularly and
in large numbers in the fecal matter
of patients with pernicious anemia,
whereas in ideal conditions of human
digestion the organism is present only
in small numbers.

Tallqvist has shown that *Dibothrio-
cephalus latus,* which may cause an
anemia similar to pernicious anemia,
contains a powerfully hemolytic lipoid
which can be extracted from the body
of the worm, and has been able to
demonstrate quite similar substances in
the mucosa of the human digestive
tract.

> In the cryptogenetic form of per-
> nicious anemia it is very exceptional
> to find free HCl in the stomach con-
> tents. In 42 cases seen in their in-
> ternal service in the University of
> Helsingfors the writers fully con-
> firmed this fact. In but one of these
> series was there free acid present.
> In the bothriocephalus type, on the
> contrary, 17 per cent. of 57 cases
> showed the presence of free HCl in

the stomach contents. After the expulsion of this tapeworm this percentage rose to 43.8 per cent. Even this figure is doubtless too low; it is at least 50 per cent., *i.e.,* in every second case of bothriocephalus anemia free HCl reappears in the stomach after the disease has been cured. Schauman and Levander (Finska Lakare. Handlingar, Feb., 1917).

The spleen is generally thought to present no characteristic lesion, although the amount of iron in it is usually increased. It may, however, be slightly enlarged, and be the seat, as observed by Stanley, of sclerotic changes, along with similar changes in the pancreas and adrenals.

Changes in the spleen and liver similar to those described by Meyer and Heinecke in man in pernicious anemia and in other severe anemias may be produced in animals by the administration of hemolytic substances; the writer's results confirm those obtained by Morris. In some instances, especially in chronic anemias with degeneration, the liver and spleen both resembled the organs of the embryo at the stage when these organs are engaged in hematopoiesis. Domarns (Archiv f. exper. Path. u. Pharm., Bd. lviii, S. 319, 1908).

Jaundice is probably due to accumulation of iron in the hepatic system. In a case studied by Ruttan and Adami, the total quantity of iron found in the liver was 0.2433 per cent. by weight calculated to the fresh undried tissue. This is equivalent to about 0.72 per cent. to the dried tissue. The estimation accords fully with the observations of previous observers, as showing the very great increase in the iron contained in the liver in this disease. Kelynack and Coutts found it to be five times greater than normal. The iron is mainly deposited about the periphery and middle zone of the lobules, and is derived from the vast number of destroyed red corpuscles. The kidneys, spleen, pancreas, hemolymph-glands are also laden with iron-pigment derived from these cells.

A study of 20 cases showed that bile pigment is frequently found in the blood in pernicious anemia, and is the cause of the jaundice. The bile pigment is in some way fixed to the plasma, and therefore does not appear in the urine. The presence of bile pigment in the blood is not always betrayed by jaundice. Bile salts are frequently found in the blood, alone or associated with bile pigment. Blankenhorn (Arch. of Internal Med., Mar., 1917).

[I have pointed out that bilirubin corresponds in its chemical properties with the adrenal principle. Hence its presence in the blood. C. E. DE M. S.]

The posterior and lateral spinal tracts present changes resembling those observed in tabes, but most marked in the posterior lateral columns, as observed by Nonne, and to a less degree in the lateral columns. All these changes are not typical of pernicious anemia, however, and may be met with in other diseases in which cachexia and marasmus predominate, such as Addison's disease and diabetes. Hemorrhagic areas in the cord and brain due to hyaline degeneration of the blood-vessels are also met with. We have seen that retinal hemorrhages constitute a diagnostic feature of the disease.

Two cases illustrating 2 of the types of nervous-system involvement. In the first case, which had the longer and more pronounced history of anemia, the nervous symptoms were at a minimum and the posterior columns of the cord, particularly in the cervical region, alone showed degeneration, characteristically patchy in distribution. In the second case, the nervous involvement, particularly in the later stages, overshadowed the anemia. Here the spinal cord pre-

sented very extensive, yet incomplete degeneration with slight replacement gliosis in the posterior columns, and also a similarly irregular, but more diffuse degeneration in the lateral tracts, which, however, was a rather less complete and apparently somewhat more recent process. Camac Milne (Amer. Jour. Med. Sci., Oct., 1910).

The writer examined the brains of 7 persons who died of primary idiopathic pernicious anemia. The most salient features in the pathologic anatomy of these brains, were the following: 1. Not only do degenerated areas of the Lichtheim type, such as are typically found in the posterior and lateral funiculi of the spinal cord in pernicious anemia patients, occur in the medullary portions of the brains of these cases, but they occur with about the same frequency, though their demonstration may be rendered more difficult. 2. Patients who show degenerative changes in the spinal cord at necropsy, usually show the same type of lesion in the brain also. 3. In addition to these focal degenerative areas found in the white matter, which may or may not be associated with blood-vessels, one also finds a diffuse degeneration, which, though it is, as a rule, somewhat more striking in the long association tracts, also occurs in the short commissural fibers passing from one gyrus to another, thus rendering the view untenable that it is the distance of these fibers from their trophic centers which is instrumental in causing the degeneration. 4. The gray matter is by no means immune from the destructive process. This is usually focal in character, and begins around the pyramidal cells of the marginal gray layer, the cells themselves being ultimately destroyed in the process, this, in turn, giving rise to a secondary and very diffuse degeneration of the medullated fibers in the white matter. 5. Though some degeneration was noted in the fibers of the internal capsule and in the long tracts passing through the pons, the degeneration at this level was less intense than that seen either in the cord or in the brain. 6. The appearance of these plaques, not only around the blood-vessels but also around some of the larger pyramidal cells, seems additional evidence that lymph stasis is an important factor in the production of these foci. 7. Well marked psychoses, such as are occasionally associated with pernicious anemia, probably have little or nothing to do with these destroyed areas. 8. The milder mental manifestations such as somnolence, apathy, and terminal delirium, are probably in a measure dependent on these lesions, though the chief causative agent of these symptoms is probably the toxin itself. Woltman (Arch. of Internal Med., June, 1918).

The bone-marrow usually presents changes which indicate abnormal activity, being composed mainly, when the case is not too far advanced, of hematoblasts, as emphasized by Rindfleisch. It resembles in this state, as noted by H. C. Wood, Pineau, and others, the hemoblastic marrow of childhood. Other changes frequently found, according to Muir, are (*a*) increased number of nucleated red corpuscles in the marrow; (*b*) transformation of the fatty marrow in the shafts of the long bones into red marrow; (*c*) absorption of the bone trabeculæ between the red marrow. Later, it presents all the signs of excessive compensatory function, being actually hypertrophied in some instances. When this stage is reached the bone-marrow may lose its power to create red corpuscles.

The proteids of the plasma may be altered in their respective proportions, and considerably reduced—40 per cent. below the average normal quantity, according to Ruttan and Adami—the globulins being especially reduced.

Although fatty degeneration is present in practically all organs, emaciation is exceptional, though the adipose tissue is pale and yellowish, contrasting with the usually red muscular tissue. The heart, however, is enlarged and flabby, and its muscular elements are pale, friable, and fatty, its cavities containing light-colored blood. The general fatty degeneration affecting markedly the vessel walls, these are extremely friable; hence, the hemorrhages, retinal, cutaneous, etc., and the ecchymoses so frequently witnessed.

DIAGNOSIS.—While pernicious anemia possesses characteristics that readily distinguish it from other blood affections,—the color of the skin, the retinal hemorrhages, etc.,—the early stages are generally such as to suggest less dangerous diseases.

Benign Anemia.—Intractability of the disease, after the removal of supposed causes and the faithful use of appropriate measures of treatment, strongly suggests pernicious anemia.

Chlorosis.—From this affection pernicious anemia may readily be differentiated by the blood examination. Instead of relative increase of hemoglobin, the presence of gigantobasts, marked oligocythemia, and macrocytes differentiate.

The erythrocytes, or red corpuscles, in chlorosis, may be normal in number and size, the only change being a deficiency of hemoglobin. Again, the corpuscles may be normal in number, but diminished in size, while the percentage of hemoglobin is normal; finally, the corpuscles may be diminished in number with either a diminished, normal, or perhaps an increased percentage of hemoglobin.

Leukemia.—This disease may be excluded by the absence of the characteristic blood-change: excess of white corpuscles.

In a case of leukemia the patient often does not show enough pallor to make the physician suspect the disease. The lips have a dirty-red color rather than a peculiar pallor. The number of white corpuscles would cause pallor in a patient with simple anemia, but in this disease the opacity of the blood is great and the pallor fails to show.

Pseudoleukemia is excluded by the absence of the affection of the lymphatic glands which characterizes this disease, more commonly known as Hodgkin's disease.

Gastric Cancer.—This condition almost always shows itself after the age of 40 years, whereas pernicious anemia is sometimes observed earlier in life. In cancer the skin is pale; in pernicious anemia the peculiar lemon color is striking in the majority of cases. While gastric symptoms and absence of hydrochloric acid are prominent features of cancer, the digestive disorder is slightly marked in anemia and examination of the gastric contents is negative. The reduction of red cells is greater in pernicious anemia than in cancer. The reduction of hemoglobin relative to corpuscles is not so great in pernicious anemia as in cancer. The average size of red cells is greater and polychromatophilia is marked.

In grave anemia in 11 cases of nephritis with uremia, the anemia masked the renal disease. The anemia seems usually the result of the uremia and fluctuates with it. Cases of pernicious anemia may be mistaken for arteriosclerosis. In doubtful cases of arteriosclerosis, especially those with a history of remissions, frequent blood counts and neurologic examinations for cord changes should

be routine procedures. Aubertin and Yacoel (Presse méd., July 10, 1920).

[It should not be forgotten that the causative toxemia in nephritis, arteriosclerosis, and other conditions may likewise produce through hemolysis all the symptoms of pernicious anemia.   S.]

Finally, increasing emaciation attends a cancerous disorder, whereas in cases of pernicious anemia the patient not only retains his adipose tissues, but sometimes becomes corpulent. In rare cases, however, there has been extreme emaciation.

The pernicious anemia of infants—a rare condition—is recognized, according to Rotch and Ladd, through the following diagnostic points: The insidious onset with moderate and paroxysmal attacks of indigestion, the extreme pallor, great loss of strength, slightly elevated temperature for months, and absence of glandular or splenic enlargements or of any demonstrable cause for a secondary anemia. The signs which are almost pathognomonic in adults lose significance, on account of the greater instability of the infant's blood-making function. Megaloblasts, normoblasts, macrocytes, and poikilocytes may occur in grave anemias other than "pernicious," yet are needed for diagnosis.

ETIOLOGY.—The main pathogenic factor, hemolysis, has been reviewed under a preceding heading; we still have to consider, however, the conditions which either predispose to the disease or are capable of causing it.

As to predisposing agencies, although the disease occasionally occurs in children and young adults, it is most common at about the age of 40 years. Males are attacked more frequently than females, with a slight difference in favor of the former. The disease is more prevalent among the

better than in the lower classes, and is most common in Europe, especially in Switzerland, e.g., in regions in which the people are badly fed and live in poorly ventilated and badly lighted houses. Fright and grief are prominent etiological factors. Syphilis, sarcoma, and other disorders capable of impairing hematopoietic functions of the bones are also capable of bringing on the disease.

According to Grawitz, the following group of etiological factors has been established: 1. Gastrointestinal disease of long standing, poor food, impaired digestion; chronic constipation, especially in women frequently pregnant; irregular defecation in women and girls, especially those of hysterical temperament. In such cases it is due to intoxication from the gastrointestinal tract. 2. Pregnancy. Here, too, probably, there is an autointoxication from the intestinal tract, on account of pressure exerted by the gravid uterus on the bowel. 3. Chronic hemorrhages, especially of small size. 4. Constitutional syphilis, particularly when associated with sclerosis of the marrow of the long bones. 5. Bad hygienic conditions of various kinds, especially in the female sex; hard work, with insufficient food, bad air, and emotional excitement. In higher social strata the disease may be found in women who are subjected to intense mental strain as the result of a desire to equal men in physical efforts. Frequent pregnancy and prolonged lactation are also factors. 6. Chronic poisoning, as, e.g., by carbon monoxide. 7. Bothriocephalus and ankylostomum —those cases belong here that are not cured after the expulsion of the worms.

Pernicious anemia is not a specific entity, but a clinical syndrome of

varying etiology. Etiologically, the disease can be considered as cryptogenetic, or of concealed origin. Under the former the writers group: (1) repeated hemorrhage (gastric, uterine, nasal, and vesical); (2) intestinal parasites (bothriocephalus and ankylostoma); (3) malaria; (4) bacterial infections; (5) tuberculosis; (6) syphilis; (7) cancer, especially gastric; (8) gastrointestinal disorders and autointoxications, which are said to be the cause of the so-called idiopathic cases; (9) nephritis; (10) pregnancy; (11) lead; (12) carbon monoxide, arsenic, and opium. The factors necessary for any of the above conditions to result in this syndrome are (a) an excessive intensity of the morbid cause; (b) the localization of the infection; (c) the duration or repetition of the cause; (d) an accumulation of the morbid condition; (e) predisposition. On the whole, progressive pernicious anemia can be the final stage of secondary anemias. Ladd and Salomon (Revue de méd., April and May, 1908).

Three cases of severe anemia witnessed due to repeated small bleedings and occasionally larger ones from varicosities situated 10 to 15 cm. above the anus which could easily be seen with the proctoscope. Destruction of these varicosities by the Paquelin cautery rapidly cured the anemia. C. A. Ewald (Berl. klin. Woch., Jan. 9, 1911).

Pregnant women represent the largest proportion of cases. Repeated parturition is probably the most prolific cause of the disease, for it is seldom met with in primiparæ. Excessive and prolonged lactation and puerperal hemorrhages and other exhausting conditions frequently appear as the primary element in the causation of the disease.

Two cases of severe anemia in pregnant women in which marked improvement followed delivery in 1 case, and by the return of the anemia at each pregnancy in the other

case. Weidenmann (Corresp. blatt f. Schweizer Aerzte, May 25, 1918).

Anemias which are met with during pregnancy differ from true pernicious anemia and seem to owe their origin to the pregnancy itself. The first symptoms are scarcely observed before the second half of pregnancy. After labor it most frequently undergoes a rapid aggravation, but in some cases it clears up. The prognosis is very grave, and medical treatment is generally ineffective. E. Petersen (Arch. mens. d'obstet. et de gynec., vii, 1, 1918).

In reporting a case the writer states that a review of the literature leads very directly to the conclusion that pregnancy and the puerperium favor the development and hasten the course of pernicious anemia. While pernicious anemia is not a disease peculiar to pregnancy it is nevertheless true that the disease occurs with unusual frequency in the course of pregnancy and the puerperium. Just what the predisposing factors are in pregnancy is not known. Prolonged lactation, frequent child-bearing, the toxemias of pregnancy, and unfavorable hygienic surroundings are factors to be reckoned with but are not conclusive. P. Findley (Trans. Amer. Gynec. Soc., May, 1918).

Certain atrophic conditions of the gastric mucous membrane, ulcers of the stomach, malaria, syphilis, cancer, and alcoholism have also been considered as etiological factors.

Pyorrhea alveolaris and carious teeth are increasingly asserting their rôle as sources of toxins which promote the disease.

Contrary to the prevailing belief and the assertions of Ehrlich and Lazarus, pernicious anemia may be a family disease.

Series of cases which all occurred in the same family—all fatal—in 2 brothers, 1 sister, a paternal cousin and a paternal uncle. Blood examinations made in all established the

diagnosis beyond a doubt. Patek (Jour. Amer. Med. Assoc., Mar. 6, 1911).

The writer observed 5 instances in one family, the father, mother, and 3 sons. C. J. Bartlett (Jour. Amer. Med. Assoc., Jan. 18, 1913).

PROGNOSIS.—The disease as a rule ends fatally and in no given case can a favorable prognosis be given. It is true that under arsenic and other measures recoveries take place, many of which last over a period of years. Relapses, however, are to be expected.

About one-half of the fatal cases last from one to six months; the remaining seldom reach beyond the second year. Periods of transitory improvement of varying duration are often a part of the natural course of the disease; so that too much importance must not be attached to the favorable results that may follow the special line of medication employed. Even if such improvement continues for a long time, the conclusion must not be too hastily reached that the disease is cured. According to Goodall, the prognosis may to a certain extent be based upon certain characteristics of the course of the blood-picture:—

1. Acute Favorable Cases.—In these the symptoms are marked; the red cells are much diminished, but show a tendency to rise; the megaloblasts are atypical and not numerous; the normoblasts are numerous; the color index is high, but tends to fall; the polychromatophilia is not marked; the percentage of polymorphonuclear cells is high; the myelocytes are absent or scanty.

Course.—A remission to a fairly normal condition may occur, which may be maintained for years.

2. Chronic Cases.—In these the symptoms are not well marked; the red cells tend to remain about one or two million; the megaloblasts are absent or scanty; the normoblasts are absent or scanty; the color index is generally low; the polychromatophilia is slight; the percentage of lymphocytes is high; the myelocytes are scanty.

Course.—The cases are apt to be chronic. The patients can work, though they feel weak, and, though febrile attacks, etc., may occur, they have little bad effect. Improvement seldom occurs, but the duration may be for several years.

3. Subacute Cases.—In these the symptoms are fairly well marked; the red cells about one million, showing slow and irregular tendency to rise; the megaloblasts are numerous; the normoblasts are less numerous than megaloblasts; the color index is high; the polychromatophilia is distinct; the percentage of lymphocytes is high in the absence of fever; the myelocytes are fairly numerous.

Course.—Symptoms improve; blood improves to a certain extent. The duration is about two years, unless complications reduce this period.

4. Acute Unfavorable Cases.—In this type the symptoms are marked, and there may be hemorrhages; the red cells are about one million, and tend to remain or go lower; the megaloblasts are typical and numerous; the normoblasts are less numerous than megaloblasts; the color index is high; the polychromatophilia is marked; the percentage of lymphocytes is high in the absence of fever; the myelocytes may be numerous.

Course.—A fatal termination is to be expected in a few months.

The tendency to relapse is in reality due to the remarkable persistence of the specific hemolytic infection underlying the disease, since it

is always accompanied by a recru-
descence of the lesions in the tongue,
stomach, or intestine, and by the
glossitic, gastric, or intestinal symp-
toms connected therewith. Hunter
(Brit. Med. Jour., Nov. 9, 1907).

The immediate prognosis in certain
cases of pernicious anemia with blood
depletion below 400,000, although
serious, is not hopeless. The prog-
nosis depends on the degree of red-
cell regeneration in the bone-marrow;
the age of the individual and the
potency of the hemolytic poison be-
ing important factors. Stone (Jour.
Amer. Med. Assoc., April 18, 1908).

Report of 3 cases of pernicious
anemia with remissions, with tabu-
lated blood-counts. In one case the
improvement followed the removal of
the patient from the county farm to
the hospital, where the better hy-
gienic and dietary conditions were
undoubtedly a strong factor. In sev-
eral cases observed, out of a total of
25 in the last two and a half years,
in which fermentative changes in the
intestines were a prominent symp-
tom, high colonic irrigations with
physiological salt solution seemed to
be connected with remissions of im-
provement. Though the blood-count
shows a marked improvement in the
remissions, there are still abnormal
features indicating that a disturbance
in hematogenic function still exists.
At best a remission is but a partial
cure, and reserve in prognosis and
caution in interpreting apparent
therapeutic results are always advis-
able. W. L. Bierring (Jour. Amer.
Med. Assoc., Aug. 1, 1908).

Case of pernicious anemia in which
there was a period of complete re-
mission of symptoms, amounting to
a cure for some sixteen years, with
final relapse showing all the charac-
teristic symptoms and pursuing a
truly progressive course to a fatal
ending. A. McPhedran (Amer. Jour.
Med. Sci., Aug., 1910).

Nägeli has reported complete re-
covery for 11 years to date in 2 cases
and for 5 years in another case. Two

of his patients bore other children
later with no return of the anemia.
The mortality is high among the chil-
dren simply because anemia brings
on premature delivery. Schuepbach
(Correspondenzbl. f. Schweizer Aerzte,
Bd. xliii, nu. 45-47, 1913).

Case in a primipara, of 22 years, in
whom the blood-picture was typical.
As a result of a spontaneous miscar-
riage she was immediately relieved of
all her symptoms. The child was
prematurely born, asphyxiated, and
died after 1½ hours. The patient re-
mained entirely free from symptoms.
Wolff (Deut. med. Woch., Mar. 26,
1914).

TREATMENT.—Arsenic cures the
curable cases and benefits the others.
Iron is worse than useless, having
shown itself injurious in several cases
reported—doubtless because the liver
is already overladen with iron. Fowl-
er's solution may be given in 3-minim
doses three times a day, increased by 1
minim daily until 30 minims are taken
after each meal, provided the stomach
does not rebel, which is seldom the
case. The patient should be watched
and the drug reduced or discontinued
temporarily on the appearance of any
of the physiological effects of arsenic:
edema of the lids, etc. In some in-
stances the doses have been increased
with marked benefit until as much as
20 drops were taken at a dose.

The cause of the hemolysis must be
carefully sought and removed. It is be-
cause this phase of the treatment of the
disease is often overlooked that its
prognosis is so unfavorable.

Considerable importance is at-
tached by the writer to oral sepsis,
particularly that known to underlie
various disorders of toxemic origin,
pyorrhea alveolaris. Carious teeth
should be removed, and, if there is
pyorrhea alveolaris, the affected teeth
taken out; if the patient's condition

does not permit, local antiseptic treatment, together with an **autogenous vaccine**, may be tried. W. H. Wilcox (Pract., Sept., 1913).

[In the article on RIGGS'S DISEASE, pyorrhea alveolaris, in the eighth volume, will be found other efficient methods for the prevention of toxemia due to this cause. S.]

The writers recommend removal of all ascertainable foci of infection, an abundant **roborant diet**, **arsenical** treatment, the administration of **hydrochloric acid** immediately after meals, and of **pancreatin** and **calcium carbonate** 3 hours after each meal. Splenectomy and transfusions of blood were not found necessary. Several of the patients thus treated have remained well over a long period. L. F. Barker and T. P. Sprunt (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 9, 1917).

The writer had 24 cases in which **operations to eliminate pathogenic foci** had been resorted to. The regions in which the foci were found were the gall-bladder, the appendix, and the mouth and throat. Of the 24 cases, 14, or 58 per cent., were all clinically in good condition after intervals since operation varying from about 7 to 32 months. This latter case is perfectly well and carries no evidence of pernicious anemia in her blood, except an occasional normoblast. In all cases except one in which the disease has recurred, the patient presented mental, nervous or spinal cord symptoms when they came under treatment, and in most of them these symptoms occurred early in the disease. It would seem that in all cases with involvement of the spinal cord and central nervous system, the prognosis is extremely bad under any form of treatment. Such patients should not be submitted to operation. Percy (Surg., Gynec. and Obstet., May, 1917).

According to Grawitz, **rest in bed** is one of the first requisites; the assimilation of food must be stimulated. The patient should be placed on a milk and vegetable **diet**. **Lavage of the stomach, intestinal irrigation,** and **saline laxatives** are useful. If the urine contains much indican **intestinal antiseptics** are indicated. He also regards **arsenic** as the best remedy; it can be given with **quinine**. Inhalations of **oxygen** have been employed with advantage. **Massage and gymnastic exercises** are often of service. After apparent recovery the patient must be carefully watched, as relapses may occur, particularly if the hygienic and dietetic conditions are unfavorable.

Case of pernicious anemia treated by Grawitz's method. The patient was a man 33 years old who was admitted to the hospital after suffering for five weeks from anemia and weakness. All the symptoms manifested by the patient were that of a typical case of pernicious anemia. Treatment consisted of a strict **diet** of milk and vegetables, daily **enemata**, with **arsenic** and **hydrochloric acid** given by the mouth. Lavage of the stomach was not performed, owing to the patient's objections. After eight weeks in the hospital and a month's holiday in the mountains his general condition was excellent. Nicolayson (Lancet, Nov. 7, 1908).

During **overfeeding**, symptomatic improvement took place with distinct betterment in the blood picture in 3 cases observed by the writer. A diet allowing from 60 to 65 calories per kilogram (approximately double the minimum requirement) is recommended, this to be given in the ratio of protein, 16 per cent.; fat, 42 per cent., and carbohydrates, 42 per cent. Peppard (Minn. Med., Sept., 1919).

When the gastric disorder, which is a usual symptom, prevents the administration of **arsenic**, the latter may be given **subcutaneously**, while the stomach is treated directly by lavage. Or, **salvarsan** or **neosalvarsan** might be tried.

In 1 of several cases in which **salvarsan** proved effective, the patient had no history of syphilis, and gave a negative Wassermann in the serum and spinal fluid before the salvarsan was given. And yet this patient, who was in his fifth relapse, quite unresponsive to Fowler's solution and only showed a very slight improvement after four months of sodium cacodylate injections, showed after the intravenous administration of salvarsan, in doses of 0.3 Gm. (5 grains), every 4 weeks, a steady rise in the blood-count. The red cells, in 16 weeks, rose from 500,000 to 5,-000,000, the hemoglobin from 23 per cent. to 90 per cent., and the patient's general condition was much improved. It is evident that it is as a powerful arsenical preparation, *i.e.*, as arsenobenzol, that salvarsan acts, and that as such it should command even greater confidence than in the past. Boggs (Bull. Johns Hopkins Hosp., xxiv, 322, 1913).

In a case of pernicious anemia with achylia gastrica refractory to Fowler's solution, symptomatic recovery occurred under a single intravenous injection of **salvarsan**. The patient gained 30 pounds in weight with a return of the blood-picture to normal, but a positive Wassermann remained in the serum and negative in the spinal fluid. It is not, therefore, as an antiluetic that salvarsan acts. W. Egbert Robertson (N. Y. Med. Jour., July 4, 1914).

It becomes a question whether **neosalvarsan** might not be preferable to salvarsan in these cases, and whether either is preferable to arsenic. The writer used small doses of salvarsan and neosalvarsan intramuscularly in 21 cases. The benefit was more prompt and the duration of the improvement generally longer than when arsenic was given by the mouth. There also seemed to be a larger proportion of apparent cures. There was usually slight local disturbance and some fever. Morphine was occasionally necessary when the pain was very troublesome. **Salvar-**

san seemed more effective than neosalvarsan, but the latter caused less local reaction. Bramwell (Brit. Med. Jour., Mar. 6, 1915).

The rate of **salvarsan** given intravenously in pernicious anemia was shown by the writer's experiences in 3 very severe cases. In all of them the alministration of small doses of salvarsan was followed by restoration of the blood-picture almost to normal, but 2 of the cases recurred later, 1 with a fatal outcome. Lampe (Med. Klinik, Nov. 19, 1916).

An excess of hydrochloric acid is not uncommonly found in the gastric secretions. In such cases Sée recommends an almost exclusive diet of meat and other albuminous foods: **raw meat** to the extent of 10 to 12 ounces daily.

In the majority of cases there is deficiency of hydrochloric acid and pepsin, especially in advanced cases. Good effects have been obtained from large doses of **hydrochloric acid** and **pepsin** under these conditions.

The great majority of cases of pernicious anemia suffer from an absence of hydrochloric acid and pepsin in the gastric secretion, and this condition is further harmful in that the essential element for pancreatic secretion is produced only under the stimulus of the acid chyme passing over the duodenal mucosa. To cause an artificial digestion, pancreatic as well as gastric, hydrochloric acid and pepsin in much larger doses than are usually considered permissible prove effective. In a personal case, the patient received 30 grains of **pepsin** and 105 minims of dilute **hydrochloric acid** three times a day, the latter being given in 15-minim doses every ten minutes in albumin water to disguise the taste. The fact that the acid was given combined instead of free did not affect its action. The further treatment consisted in daily **irrigations of the colon** and a liberal **mixed diet.** It was shown from the

blood examination that the treatment had been followed by most satisfactory results. Julius Rudisch (Med. Rec., March 5, 1910).

Croftan, of Chicago, found that 15 drops of the strong hydrochloric acid after each meal procured notable improvement in 14 cases, the symptoms of pernicious anemia disappearing while those of achylia persisted. The writer recommends Croftan's treatment in all cases showing reduced gastric acidity. He gives 10 to 15 drops of the acid in mucilage water a few minutes after each meal, the dose being repeated in 30 minutes. The mucilage water, which is employed to prevent injury to the gastric mucosa by the acid, consists of 1 ounce (30 Gm.) of pulverized acacia to 1 quart (1000 c.c.) of water. One-half glassful of the mucilage water is used to each dose of acid. He deems it important to regulate carefully the dose, for if too little is given the patient will not reap the benefit of the treatment, while if too much is given he will not retain the remedy. J. A. Sealy (Lancet-Clinic, Feb. 15, 1913).

The use of **bone-marrow,** introduced by Fraser, has given good results in some cases and no results whatever in others. Freshly prepared each day with an equal quantity of glycerin, red marrow, 1 or 2 ounces daily, has seemed to give the best results. It should be tried only where arsenic has failed.

Transfusion of blood should never be omitted when improvement does not follow the administration of arsenic. The best method is that employed by Brakenridge, of Edinburgh. The blood is kept fluid by admixture with one-third part of its bulk of a 1 : 20 (5 per cent.) solution of phosphate of soda in distilled water kept at blood heat. John Duncan, who performed the transfusions in Brakenridge's cases, insists upon the necessity of slowness in operating. He regards thirty minutes as the minimum time that should be occupied in injecting 8 ounces of fluid.

Series of 26 cases treated by **transfusion** at the Mayo Clinic. Forty-six transfusions were performed in the series, a single transfusion proving sufficient in only 11 patients. Sixty-nine per cent. of the entire series received marked immediate benefit from the procedure. Among 14 unfavorable cases deemed unsuitable for splenectomy similar improvement was noted in 50 per cent. Up to the sixth decade, the age of the patient had no bearing on the results; of 5 patients between 60 and 70 but 1 showed definite improvement. Patients with a history of remissions, even though ill for several years, seemed most benefited by transfusion. Those without remissions often failed to respond. Recent, acute cases were usually little influenced. Results following transfusion from relatives were not superior to those in the cases of unrelated donors. But 1 patient had a severe reaction; mild fever and a severe chill lasting 40 minutes followed transfusions from the wife and from a friend; no benefit resulted. Eleven patients had mild fever for a day or 2. Such reactions did not prove necessarily indicative of benefit from the procedure. General improvement usually paralleled that in the hemoglobin. Distressing numbness, burning, and tingling of the hands and feet were relieved by the treatment. When no benefit follows a transfusion, a different donor should be tried. A. Archibald (St. Paul Med. Jour., Feb., 1917).

Massive **transfusions** of blood offer the greatest chance of improvement to sufferers from pernicious anemia, but any error in the technique may be followed by a fatal result. The procedure is one which should be attempted only by those who have had considerable experience in intravenous injections and are well acquainted with the physiological teachings

about clotting of blood. Even with perfectly matched bloods reactions may occur, but they may be prevented by the administration half an hour before the injection of $\frac{1}{150}$ grain (0.0004 Gm.) of **hyoscine methyl bromide** along with ⅙ grain (0.01 Gm.) of **morphine.** O. Leyton (Pract., Mar. 1917).

The writer observed 2 cases of pernicious anemia in infants of 11 and 5 months from private practice. He has previously published 2 personal cases, and found 56 cases in the literature. This includes 32 cases in which the anemia was traceable to the bothriocephalus or a tenia. Only 2 cases are known of essential progressive pernicious anemia in older children. The serum used was obtained by venesection of animals at the height of the regeneration of blood following a previous extensive withdrawal of blood. This **hematopoietic serum** seems to have a decidedly favorable action on the composition of the blood, when injected in cases of pernicious anemia. These infants were given daily subcutaneous injections of 5 or 10 c.c. of the serum. The changes in the blood were from hemoglobin 20 per cent. and reds 658,875, to 53 per cent. and 2,102,125 reds in 9 months, indicate the practical efficacy of this form of serotherapy. A. D'Espine (Revue Médicale de la Suisse Romande, Aug., 1918).

Transfusion offers more for progressive pernicious anemia than any other form of treatment.

The theory of toxic hemolysis is accepted to explain the genesis of the disease.

It is highly probable that transfusion of blood owes its beneficial effects to the stimulation of the antihemolytic properties of whole blood, although the possibility of its power to increase the functional activity of the bone marrow should also be recollected.

In a case seen by the writer in consultation transfusion produced a prompt remission lasting seven months, after the patient was thought to be lost. A second transfusion was followed by a remission, though less promptly, and at the time of writing, more than one year after the first transfusion, the patient declared that he had not "felt so well for 15 years." The blood picture, as well as the general health, were greatly improved by both transfusions. J. M. Anders (Trans. Assoc. Amer. Phys.; Med. Rec., Sept. 6, 1919).

Daily findings reported as to the blood and urobilinemia after **transfusion** of 900 c.c. of blood drawn into 120 c.c of a 2 per cent. solution of sodium citrate in a man of 33 with pernicious anemia during his third attack. In 2 weeks the erythrocytes had increased from 850,000 to 3,118,-000; the hemoglobin from 19 to 66 per cent.; the bile pigment in the blood serum had dropped from 45 to 7, and the urobilin figure from 875 (4500 the second day after the infusion) to 42. The improvement progressed for a time, but the man returned about 4 months later in his fourth attack, the erythrocytes having dropped to 1,382,000 and the hemoglobin to 28 per cent. Scheel and Bang (Norsk Mag. f. Laegevidensk., Mar., 1920).

Defibrinated blood has been used **subcutaneously** by Westphalen with success.

Subcutaneous injections of **normal saline solution** every alternate day, and on the intervening **saline enemata,** with **arsenic** internally, have been recommended by McPhedran.

Intestinal antiseptics have been recommended. Hunter holds that the best intestinal antiseptic is **betanaphthol** and **salol,** along with **arsenic** when that can be borne. I consider **thymol** entitled to the first position, a fact which seems to be more fully appreciated in Italy than elsewhere. In accordance with the view that pernicious anemia is due to the absorption

from the intestine of substances foreign to the healthy body, and destructive to the red corpuscles, its treatment by intestinal antiseptics is certainly most rational.

When the disease is due to the *Ankylostoma duodenale*, **thymol**, 2 to 3 drams daily, is a very effective vermicide, according to Bozzolo.

> Two cases due to *Bothriocephalus latus*, the infection being accompanied by the severest kind of anemia. In one patient the red corpuscles fell to 780,000 and the hemoglobin to 15 per cent. The second case was even more severe the red corpuscles falling to 660,000 and the hemoglobin to 10 per cent. Hemorrhages were noted along the veins of the retina. The improvement in both cases after **thymol** treatment was marvelous, and in the second patient in thirteen days the number of red corpuscles trebled. A. Meyer (Med. News, April 8, 1905).

Herter recommends frequent and thorough **irrigation of the colon,** since it is the chief thriving place of the anaërobic bacteria which cause the specific putrefaction. Following this suggestion, Dittmar and Hollis were able to report a few months ago recovery in 2 cases of pernicious anemia by irrigation of the colon which had resisted all other methods of treatment.

> In all cases of pernicious anemia, the stools should be examined to determine the presence of a *Bacillus capsulatus aërogenes* infection. If these bacteria are present in great quantities, then **high irrigation**, combined with **arsenic** internally, should be used; and if the patient fails to improve then the appendix offers the best route for thorough irrigation. Lucius E. Burch (Jour. Amer. Med. Assoc., March 13, 1909).
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> When the *Bacillus capsulatus aërogenes* or the percentage of anaërobic bacteria found in evacuations from bowels is large, then, after thorough trial at colonic irrigation and failure

to improve the symptoms or to lessen the percentage of bacteria, the operation of **appendicostomy** is warranted. J. A. Witherspoon (Southern Med. Jour., July, 1909).

Cholesterin has been introduced into the therapy of pernicious anemia because of Ransom's finding that it prevented the hemolytic effects of some substances, such as saponin and cobra poison. A 3 per cent. solution of cholesterin in oil is given in 100-Gm. (3⅓ ounces) doses daily. It is apt, however, to disagree with the patient.

> Three cases of pernicious anemia and 1 of secondary anemia referable to nephritis in which **cholesterin** was used for therapeutic purposes, the aim being to counteract any hemolysins that might be active in a manner analogous to the action of cholesterin on cobra lecithide. Of the 3 cases, one patient remained unimproved, while in the other two cholesterin was decidedly beneficial. The latter case was in a wretched condition, with intense dyspnea, ascites, pleural effusion, edema, and a red count of 750,000 with 18 per cent. of hemoglobin. After a week the count had risen to 1,750,000 and the hemoglobin to 30 per cent., while the threatening symptoms had all disappeared. The improvement was thus quite remarkable, but after a few weeks no further gain was obtained and still later a relapse occurred which ended fatally. Reicher (Berl. klin. Woch., Nu. 41-42, 1908).
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> When cases prove refractory to arsenic the writer found cholesterin efficient in daily doses of 1 to 2 Gm. (15 to 30 grains) administered in cachets or oily solution. M. Roch (N. Y. Med. Jour., Mar. 8, 1913).

Glycerin has also been tried in parasitic pernicious anemia, as a result of Tallqvist and Faust's suggestion that glycerin might combine with the lipoid substance assumed to be responsible

for the disintegration of the red corpuscles and thus combine to form a harmless product. The special lipoid substance found in the anemia from intestinal parasites proved to be oleic acid, and this combines with glycerin to form triolein.

> In the first of 2 cases in which **glycerin** was tried, the result was very encouraging, and in the second administration of 3 tablespoonfuls of glycerin a day, with lemon juice, was followed in the course of two and a half months by an increase in the red corpuscles from 990,000 to 4,760,000, and of hemoglobin from 20 to 90 per cent. No other drugs were given except a little antipyrin and caffein for a day or so to combat a neuralgic headache. Vetlesen (Norsk Mag. f. Laeger, Oct., 1909).

Operative treatment of pernicious anemia was introduced by Eppinger, of Vienna, **splenectomy** having first been performed by this surgeon in 1913 on the sound plea that the red cells were chiefly destroyed in the spleen. As Thayer states, however, it seems a serious matter to expose the patient to the extra danger of so severe an operation, when, as is well known, some patients may live years without operative intervention.

> The mortality of **splenectomy** appears to be about 11 per cent. The best results of splenectomy are said to be obtained in the treatment of hemolytic jaundice. Eliot and Kavanel in 48 cases collected in 1915 reported only 2 deaths, a mortality of 4.2 per cent. Krumbhaar in 1916 had collected 156 cases of pernicious anemia treated by splenectomy with 30 deaths. The Mayo Clinic reported 32 splenectomies for pernicious anemia up to April 1, 1916, with 3 deaths, or 9.7 per cent. mortality. Of the survivors, 22 or 78 per cent., showed continued improvement; of 16 followed up for 6 months, 11 continued to improve and 3 had relapses. From

the experience of the Mayo Clinic it would seem that splenectomy should be considered where the patient is youthful and middle aged, where he shows good general resistance, where splenic enlargement is of moderate degree, and where there is evidence of hemolytic action.

The treatment of pernicious anemia by splenectomy is still on trial and is apparently merely palliative. There is, however, reasonable hope for improved results. J. B. Deaver (Phila. Co. Med. Soc.; N. Y. Med. Jour., July 27, 1918).

> Among 50 cases of pernicious anemia treated by **splenectomy** more than 3 years before, the writers found that 10 patients (21.3 per cent.) of those who had recovered from the operation survived splenectomy 3 years or longer. Five patients (10.6 per cent.) had survived more than 4½ years. In addition to the immediate remission which occurred constantly following splenectomy, splenectomy prolonged life in at least 20 per cent. of the cases. The patient shows a more marked immediate improvement in the type of case in which there is evidence of active hemolysis. Splenectomy may be recommended in pernicious anemia when, in view of all the circumstances, personal as well as medical, the possibility of prolongation of life appeals to the family and patient. Occasionally it may be performed to bring about an immediate remission. Giffin and Szlapka (Jour. Amer. Med. Assoc., Jan. 29, 1921).

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ANEMIA, SECONDARY, OR SYMPTOMATIC. —DEFINITION.—A deficiency either in the quantity or the quality of the blood, affecting the blood mass or the cellular and albuminous constituents. Genuine secondary anemia is essentially a symp-

tomatic disorder, referable to obvious pathological conditions, which deplete the blood volume, diminish the number of erythrocytes, and reduce the amount of hemoglobin and albumin.

> When summed up all cases of anemia include very few of the so-called primary anemias and a great many forms of secondary anemia. The secondary or simple anemias, analyzed from the standpoint of cause, might be grouped under: 1, infections; 2, those following hemorrhage, manifest or concealed; 3, those due to some form of intoxication, in these days new poisons are being encountered, and cases, such as had been termed pernicious anemia, might be due to TNT poisoning; 4, parasitic anemia; 5, anemias that were expressive of some deep seated, perhaps overlooked, neoplasm. Alfred Stengel (Trans. Phila. Co. Med. Soc.; N. Y. Med. Jour., July 27, 1918).

TYPES OF SECONDARY ANEMIA.—It is convenient to classify the simple secondary anemias into several clinical groups which relate directly to the predominant factor active in the individual case. While a classification of this sort must needs be imperfect, for frequently several factors are concerned in a single instance, it will serve to designate the important underlying condition of which the blood impoverishment is symptomatic. The following groups are sufficient for the inclusion of all anemias of secondary origin. I, posthemorrhagic; II, infectious and toxic, and III, trophic.

I. **Posthemorrhagic anemias** comprise that varied class of cases directly traceable to bleeding, irrespective of its extent, duration, and character. In this group, therefore, are included the acute anemias due to loss of blood by trauma, operation, abortion, par-

turition, epistaxis, hemoptysis, gastric and intestinal ulcer and neoplasm, hemorrhagic pancreatitis, and under the same heading are the grave anemias consecutive to the rupture of an aneurism, of a Fallopian tube, and of a large mass of varicose veins. The hemorrhagic diseases (purpura, hemophilia, scurvy), hemorrhoids, and uterine fibroids, all of which are capable of causing persistent, though perhaps moderate, loss of blood, may also excite a secondary anemia, perhaps of pronounced severity.

> Various authors have described certain differences which they deemed to be fundamental, but the experiments of the writer indicate that although there are minor differences, all the essential features of anemia produced by toxins can be produced by hemorrhage. Milne (Jour, Exper. Med., Sept., 1912).

> In a comprehensive study of **blood transfusion** in the treatment of severe posthemorrhagic anemia and the hemorrhagic diseases, the writer found that in acute and chronic posthemorrhagic anemia, no other remedy would compare in efficiency with whole blood in producing hematopoietic stimulation. In the acute variety (following trauma, labor, operation, or accidental cause, or as complication of ectopic pregnancy, gastric or duodenal ulcer, typhoid fever, etc.) a single large transfusion is indicated, while in the chronic type (that resulting from repeated small losses of blood) better results are obtained by giving serial transfusions of small or moderate amounts of blood. E. W. Peterson (Med. Rec., Apr. 15, 1916).

II. **Infectious and toxic anemias** develop chiefly as the result of hemolytic agencies, and are encountered in the specific infections, malignant disease, intestinal helminthiasis; in poisoning by certain so-called blood

poisons—nitrobenzol, potassium chlorate, lead, mercury, arsenic, antimony; and in states of autointoxication— uremia, cholemia, pregnancy. Of the acute febrile infections that account for anemia of moderate intensity, enteric fever, sepsis, variola, erysipelas, rheumatic fever, and scarlatina may be named as typical examples. The anemia excited by malignant neoplasms is attributable partly to the action of circulating tumor-toxins and partly to concomitant factors, such as hemorrhage, ulceration, and interference with nutrition, as in esophageal and gastric growths. The anemia of helminthiasis is due principally to the hemolytic action of poisonous substances elaborated by the worm, notably in the case of uncinariasis and bothriocephalus disease, and to a less extent in persons harboring oxyurides, ascarides, and filariæ. Helminthiasis anemia is also favored by the associated gastrointestinal disorders, and, in uncinariasis, the parasites suck blood from the intestinal vessels of the host and pour out an absorbable anticoagulant material which may act deleteriously upon the circulating blood-cells. The luetic virus materially damages the hemoglobin and erythrocytes, and syphilitics as a class are subject to a form of toxic anemia which as a rule attains its greatest development during the tertiary stage of the infection. In malarial fever it is probable that the presence of a circulating specific malarial toxin, produced by myriads of parasites, has much to do with provoking the attendant anemia, and it is certain that in this infection the blood must suffer from the wholesale destruction of parasitiferous erythrocytes.

Report of experiments showing that vitiated air can cause anemia in human beings only when there is some predisposition of a toxic order to influence the blood-making organs. The bad air of prisons, workshops, etc., causes only pseudoanemia, i.e., pallor of the integument, but no changes in the blood. Krotkoff (Roussky Vratch, Jan. 18, 1914).

Aplastic anemia in young persons is the result of the exhaustion of function of a bone marrow congenitally defective in power of endurance, in older persons it is the result of some poison or poisons which, acting on the bone marrow, destroys its function and leads to death. A pathologic hemolysis as an essential part of this syndrome has not been shown. Rennie (Med. Jour. of Australia, June 14, 1919).

In a case reported by the writer, exposure to the X-rays for about 15 years was considered to be the cause of the anemia. It was of short duration, the patient succumbing in about 6 months, and symptoms were complained of only during the last 2 months. The rapid diminution in the red and white corpuscles was very noticeable, the reds disappearing at the rate of, roughly, 250,000 per week, and the whites sinking to 840. The color index was never over 0.9. The differential count was remarkable: Polynuclears, 41 per cent; lymphocytes, large, 54 per cent.; small, 4 per cent.; eosinophiles and basophiles, none. Larkins (Lancet, Apr. 16, 1921).

III. **Trophic anemias,** or those of nutritional origin, are met with commonly in subjects that suffer from chronic malnutrition due to faults in the quantity and quality of their food, to defective absorption and assimilation, or to a combination of these two causes, and in many such instances deficient air and sunshine, lack of exercise, confining occupation, and unsanitary surroundings must likewise be reckoned with as contrib-

uting elements. Drains upon the albumins of the system, as in habitual nephritis, persistent suppuration, prolonged lactation, and chronic dysentery, ultimately provoke well-defined, stubborn anemia of the trophic type.

Von Jaksch's anemia belongs to the category of trophic anemias. In 1889 von Jaksch described a case of leucemia in a child of 14 months, and in the following year he reported 3 cases of enlarged spleen in children, a condition which he called anemia pseudoleucemica infantum. This was characterized by a diminution in the hemoglobin and in the number of red cells, marked persistent leucocytosis, sometimes glandular enlargement, slight enlargement of the liver, a marked enlargement of the spleen, which was out of all proportion to the size of the liver, and a tendency to recovery. The blood-picture is characterized by a great diminution in the red cells and the hemoglobin, and a persistent leucocytosis. Most of the patients show a definite tendency to recover. The abnormal blood-picture in those who lived might persist for a very long period of time. This form of anemia is frequently associated with rickets. The symptoms are those of anemia in general, pallor, edema, weakness, dyspnea, etc. a large liver, and a very large spleen, with a characteristic blood-picture. The onset is gradual and the patient is usually brought in for treatment when a well marked enlargement of the spleen has developed.

After tuberculosis, diphtheria and the eruptive diseases, **Leishman's anemia** or leishmaniosis is the most prevalent disease in southern Italy. Families living in rural districts or having much to do with domestic animals are specially subject to it. Direct contagion can be incriminated in most of the cases, the parasite probably being transmitted by means of bedbugs. There is also much to sustain the view that dogs and dog fleas are responsible for its transmission. Franchini has recently found the parasites in gnats. G. Caronia

(Archiv f. Kinderheilk, Bd. lix, Nu. 5-6, 1913).

Aplastic anemia develops as hemorrhagic purpura which continues a steadily progressive course until the patient succumbs to the anemia in the course of a few weeks or months. In the case of a woman of 33 the patient had contracted syphilis 14 years before but was apparently in perfect health when given an additional mild course of mercury and salvarsan. Eight days after its conclusion the hemorrhagic purpura developed and progressed to a fatal termination in 15 days. In this, as in all the cases on record, the small numbers or total absence of blood-platelets was a striking feature of the case. E. Frank (Berl. klin. Woch., Sept. 13, 1915).

School Children's. — The writer studied 42 cases of a form of anemia found in school children characterized by *eosinophilia*. Various parasites were always present in the feces. The degree of eosinophilia is uninfluenced by the kind of parasite present. He advises, therefore, that in all cases of anemia in school children the blood should be carefully examined for eosinophilia and the stools be searched for the ova of intestinal worms. Scaroni (Gaz. degli Osped. e delle Clin., Jan. 7, 1917).

PATHOLOGY.—The principal pathologic alterations incident to anemias of the secondary type relate to the composition of the circulating blood and to the histology of the bone-marrow, of which the former changes are the more important, and, obviously, more readily available to the clinician. The blood changes vary within wide limits, depending upon the grade and the chronicity of the individual case; but in general it may be stated that they are of very moderate intensity in the average example of general symptomatic anemia. There is a more or less decided diminution in the number

of erythrocytes (*oligocythemia*), with a tolerably proportionate reduction in the percentage of hemoglobin (*oligochromemia*), and, in severe cases, one observes structural changes implicating the erythrocytes' stroma and eventually leading to the production of corpuscular deformities of shape (*poikilocytosis*), and of size (*megalocytosis; microcytosis*). Not always, however, is the hemoglobin-erythrocyte reduction proportionate, for in some forms of secondary anemia the hemoglobulin loss is greatly disproportionate to that of the cells, as, for example, in so-called "syphilitic chlorosis," which, hematologically, counterfeits maiden's chlorosis; on the contrary, in other types the erythrocytes suffer chiefly, as in that variety of parasitic anemia provoked by the *Bothriocephalus latus*, which apes true pernicious anemia in every detail of the blood-picture. These facts call for great caution in attempting to diagnose a secondary anemia by the blood changes alone, without due regard for the discovery of some adequate causal factor to be correlated therewith. In active, severe cases of anemia young, nucleated erythrocytes (*normoblasts*) escape prematurely from the bone-marrow and appear in the circulating blood in limited numbers, and in the event of intense retrograde marrow changes an occasional nucleated corpuscle of fetal type (*megaloblast*) also may be observed. With such evidences of high-grade blood deterioration one also meets with cells disfigured by atypical staining proclivities (*polychromatophilia*), and with cells whose protoplasm is stippled with fine and coarse basic granules (*granular basophilia*), both of which abnormal findings point to a considerable degree of stroma degeneration, whereby the affected cells no longer react toward acid aniline dyes, as they do normally, but show a selective affinity for basic colors, by which the stroma of the healthy red corpuscle is never stained, when exposed to a mixture containing both acid and basic dyes. The behavior of the leucocytes in secondary anemias is most inconstant. In chronic cases, especially those due to trophic defects, and in certain of the slowly progressive toxic anemias the leucocyte count does not deviate from normal, or, if it shows any appreciable change, becomes subnormal (*leucopenia*). In these leucopenic anemias it is also the rule to find a disproportionately high percentage of lymphocytes (*relative lymphocytosis*), these cells increasing in number chiefly at the expense of the polynuclear forms.

> The writer considers a high bilirubin content of the blood serum as an instructive sign of abnormal hemolysis. That the spleen is the main seat of destruction of red corpuscles has been confirmed anew by his and Daniels' recent experimental research with injections of hemolytic serum into rabbits before and after splenectomy. The latter protected the animals against the hemolysis to a great extent. The hemoglobin released from the corpuscles destroyed in the spleen is carried along the portal vein to the liver, where it is split up into bilirubin. L. S. Hannema (Nederlandsch Tijdsch. v. Geneeskunde, Nov. 3, 1917).

Other anemic blood changes, of very minor importance, comprise increased rapidity of clotting and subnormal specific gravity values.

Anemia appearing in the face of active hemorrhage, of acute infectious processes, and of malignant disease is ordinarily attended by a leucocyte

increase affecting mainly the poly-nuclear cells (*polynuclear neutrophile leucocytosis*), and in helminthetic dis-eases of recent origin there is a very constant increase in the percentage of eosinophile cells (*polynuclear eosino-phile leucocytosis*). The presence of small numbers of immature polynuclear neutrophile cells (*myelocytes*) in the blood is frequently noted in many of the severer anemias of symptomatic character, irrespective of the presence or absence of a leucocytosis.

The bone-marrow in a severe case of anemia undergoes a moderate de-gree of softening and acquires a some-what reddish hue, the attendant his-tological changes of this transforma-tion consisting of a hyperplasia of the lymphoid elements and a diminution in the number of fat-cells, which are replaced by marrow-cells or myelo-cytes charged with neutrophilic and eosinophilic granulations. Nucleated erythrocytes or erythroblasts, chiefly of the normoblastic type, are numer-ous when active powers of hemo-genesis persist. H. C. Bunting's studies of the blood and bone-marrow in rabbits rendered anemic by the injection of hemolytic poisons has thrown a clear light upon the dif-ference between the marrow changes incident to anemias of different grades of development. This investi-gator showed that hemolytic anemia excited by saponin is associated with more or less effectual depletion of the marrow-centers wherein prolifera-tion of the blood-cells takes place, and with fragmentation and other degenerative changes in the other marrow-cells, the blood-picture be-traying this grave myeloid lesion virtually corresponding to that of true pernicious anemia in man. In

contrast to these findings, posthemor-rhagic anemia, despite the presence of characteristic changes in the pe-ripheral blood, does not affect the in-tegrity of erythrogenic and leucogenic centers of the marrow. Furthermore, it would appear that in some in-stances the proliferating centers of the marrow become quite replaced by scar tissue, in which event the hematopoietic function, now impos-sible for the crippled marrow to carry on, is undertaken by the spleen.

The visceral changes to be noted in cases of chronic secondary anemia in-clude granular degeneration of the liver, kidney, and heart, and, in some instances, fatty changes in these organs. These lesions depend more upon concomitant disturbances, such as toxemia and nutritional faults, than upon the effect of the anemia *per se*, and it seems within the bounds of reason to assume that they arise in part from an undue visceral activ-ity excited by the organism's attempt to maintain a normal process of oxidation.

The liver, the spleen, and fre-quently the lymph-nodes assume a fetal type in grave or pernicious ane-mias as far as their cellular charac-ter is concerned. Erythroblastic cells and newly formed leucocytes appear in them, while the blood-making or-gan of the adult, the bone-marrow, shows likewise a picture of greatly increased activity. The writer, to-gether with Heinecke, has interpreted these phenomena as reparative in nature in opposition to another con-ception of the findings which seeks to interpret them as the primary re-sult of some unknown harmful agent. Von Domarus has greatly strength-ened the standpoint maintained by the writer by producing experimental anemias in animals and showing that the changes in the blood-making or-

gans of intrauterine as well as of extrauterine life were similar in these animals to those observed in patients with pernicious anemia. Meyer (Münch. med. Woch., June 2, 1908).

SYMPTOMATOLOGY. — Pallor, the suggestive hallmark of all anemias, is usually well marked in the secondary type of this affection, and the subject's skin, mucosa, and nails may become so blanched as to appear almost colorless. In other instances, the loss of color is much more moderate, and in still others the actual pallor is more or less obscured by a yellowish or muddy or icteroid staining of the integument. In passing, it may be remarked that pallor of itself does not justify a diagnosis of anemia, for many persons with unnaturally pale faces have a perfectly normal blood-picture, in view of which the blood examination must invariably be the court of final appeal.

Aside from pallor, the most conspicuous symptom groups in anemia are attributable to disturbances of the cardiovascular, the gastrointestinal, and the nervous systems. Of the circulatory symptoms, dyspnea, cardiac palpitation, and dropsical swelling of the ankles and legs are likely to prove sources of great distress to the patient, while the discovery of hemic murmurs at the base of the heart and of a venous hum at the root of the neck affords findings of the utmost pertinence. These anemic murmurs, generally situated at or near the pulmonic orifice, are almost invariably systolic in time and restricted to the precordial area or to its immediate vicinity. They are sometimes associated with a perceptible increase in the size of the cardiac

outline, indicative of dilatation of the heart from defective myocardial nutrition, overstrain, and, exceptionally, fatty degeneration.

The distinct positive venous pulse observed in endocarditis is not an uncommon symptom of anemia and is due to a relative muscular insufficiency of the tricuspid orifice. The cause is the same as that of the mitral insufficiency so common in chlorosis. In order to make sure of the functional character of the condition it is important to bear in mind that a relative tricuspid insufficiency in anemia develops at the same time as the mitral insufficiency, while in endocarditis the tricuspid lesion usually develops long after the mitral. Besides, disturbances of compensation are usually absent. Von Leube (Zeit. f. klin. Med., Bd. lvii, Nu. 3-4, 1905).

The foregoing symptoms, which are prominent only in severe anemias, promptly vanish as the normal composition of the blood is regained, and frequently in such cases the pulse is inordinately rapid, of low tension, and subject to arrhythmic disturbances, while occasionally the abrupt, jerky beat of the Corrigan pulse is superficially imitated.

Murmurs are audible *inside the skull* in anemia from any cause and grow less and less audible as the blood-supply returns to normal. In about 50 patients the murmurs were often distinct in hemorrhagic gastric ulcer or cancer, in pernicious anemia and with lesions localized in the skull. They were more pronounced with abnormally low hemoglobin content than with low corpuscle count. H. Koster (Zentralbl. f. innere Med., Nov. 15, 1913).

Of the symptoms referable to the gastrointestinal tract, anorexia, pyrosis, abdominal distention, sensitiveness, and unrest, nausea, and constipation may

attract attention. In the average case of secondary anemia the motor powers of the stomach are unaltered, and the secretion of hydrochloric acid remains normal or is even increased. On the other hand, there is a decided tendency toward weakening the intestinal motor function, although the juices of the gut flow naturally (Boas, v. Noorden).

Ulcers in the throat may be due to anemia or lowered vitality. The writer has seen 3 cases; all in young women. The ulcer is round, small, with scanty secretion. There was no history of either tuberculosis or syphilis and no swelling of the glands. Pohly (N. Y. Med. Jour., Aug. 27, 1910).

The *anemic vomiting* in anemic girls is apt to be mistaken for gastric ulcer. The symptoms are pain in the epigastrium and vomiting excited by almost everything that is placed in the stomach. Its mucous membrane is so hyperesthetic that whatever touches it causes pain and vomiting. This is often associated with pain and tenderness of the skin and muscles under the left breast, though there is nothing the matter with these structures. Whereas in ulcer solid food gives more pain than liquid, in anemic vomiting the pain and vomiting have not a constant relation to meals; they may have some of their worst attacks apart from food altogether. Sudden exertion, or being tired out, will bring on the same pain. Beddard (Pract., Mar., 1912).

Of the various nervous disturbances, headache, vertigo, syncope, insomnia, phosphenes, muscæ volitantes, and tinnitus aurium are familiar examples. Moderate, irregular fever is occasionally observed as a consequence of nervous factors and as a sign of septic processes. Most anemics, particularly those of chronic character, complain of unnatural fatigue, both mental and muscular, and in severe cases the patient may be incapable of sustained intellectual effort, exhibits curious mental caprices and irritability, and develops a myasthenia amounting almost to complete debility.

Six cases of anemia of the central nervous system resulting in sclerosis of the cord. The onset of the disease is gradual. The symptoms are very variable as are the changes in the spinal cord. Sometimes the posterior columns are involved; sometimes the lateral tracts are added; again, there is a diffuse sclerosis of the entire cord. Paresthesia and ataxia may persist for years with few changes in the cord, or the intensity of the alterations may be much greater than the clinical symptoms. The mental state may be dull and inattentive, and there may be various muscular palsies of eye muscles or face. Leopold (Med. Rec., Mar. 5, 1910).

The blood-picture of secondary anemia is in no wise distinctive, as already pointed out in the remarks on the pathology of this affection. Usually there is a moderate and roughly parallel loss of hemoglobin and erythrocytes, the former being diminished approximately 45 per cent. and the latter 30 per cent. below the normal standard, in the case of average severity. The stained film generally shows nothing more than simple pallor of the erythrocytes with, perhaps, a few misshapen cells and some tendency toward irregularity in their diameter measurements. Normoblasts and erythrocytes with stroma degeneration are met with only in anemias of great intensity, characterized by excessive destruction of the cells, and under such conditions an occasional megaloblast, indicating a fetal reversion of the marrow, may enter the blood-stream.

Leucocytosis, developing under the circumstances referred to in a preceding paragraph, means stimulation of the marrow's functional activity, the exhibition of which is regulated largely by the nature of the exciting cause and by the individual peculiarities dominant in the case under consideration. The coagulation-time (*hematopexis*) of the blood is shortened in close relation with the degree of existing anemia.

> The blood lipoid values in anemia were found by the writers to be normal, or nearly so, as long as the percentage of blood corpuscles remained above half the normal value. When the percentage was below this level abnormalities appeared which, in the order of their magnitude and also of the frequency of their occurrence were (1) high fat in the plasma, (2) low cholesterol in the plasma and occasionally in the corpuscles, and (3) low lecithin in the plasma. The lipoid composition of the corpuscles was found to be normal in practically every case. Bloor and MacPherson (Jour. Biol. Chemistry, July, 1917).

DIAGNOSIS.—The diagnosis of secondary anemia invariably must be based upon a suggestive blood picture plus the discovery of some factor responsible therefor. Given a blood poor in hemoglobin and erythrocytes in an individual suffering, for instance, with sepsis or gastric cancer or rheumatic fever, the diagnosis can tax no one's intelligence. But given an obscure etiologic factor in an anemic person, one must carefully interrogate through a long list of potential causes of blood impoverishment in order to detect a satisfactory cause. The differential diagnosis of secondary anemia includes the consideration of pseudoanemia, chlorosis, pernicious anemia, splenic anemia, leukemia, chloroma, and Hodgkin's disease.

Pseudoanemia versus *true anemia* is a differentiation constantly to be borne in mind in examining a patient for the first time. Spurious anemia, which, of course, shows a normal blood report, is characterized by unnatural pallor of the skin and mucous surfaces, probably of hereditary origin and explainable on the grounds of a deficiency of skin pigment and abnormal constriction of the superficial capillary network. Apart from pallor, the affection is quite symptomless. In this connection may be mentioned an angiospastic type of pseudoanemia, recognized by the abrupt appearance of attacks of transient grayish pallor induced by emotion, fatigue, exposure to cold, and similar vasomotor stimuli.

Chlorosis, though its blood picture may be precisely counterfeited by certain forms of secondary anemia (such as *Chlorosis, q.v.*), is readily distinguished from the latter by its occurrence exclusively in girls and in young women who exhibit, with passable fidelity, a varied train of unmistakable chlorotic stigmata—greenish pallor, menstrual disturbances, perverted appetite, indigestion, constipation, slight enlargement of the thyroid gland, and many symptoms referable to functional neuroses.

Pernicious anemia in its typical form gives rise to three most pertinent blood changes: extreme oligocythemia combined with a disproportionately slighter oligochromemia; the presence of numerous erythroblasts, of which cells those of a megaloblastic type predominate; and many deformed and otherwise degenerate erythrocytes, notably megalocytes and basophilic corpuscles. The first

detail of this blood-picture means that the hemoglobin content of the erythrocytes (*color index*) is unnaturally high; the second indicates active compensatory hemogenesis and fetal reversion of the bone-marrow, and the last points to the manufacture by the marrow of numerous faultily formed, functionless erythrocytes, of little or no use as oxygen carriers. Leucopenia, relative lymphocytosis, and a moderate degree of myelocytosis are among the other hematological features of this disease. In addition to these findings, it must be recalled that true pernicious anemia arises insidiously, is entirely unconnected with any tangible causal factor, and invariably progresses steadily, perhaps with temporary periods of remission, to a fatal termination. An *aplastic type* of pernicious anemia has been described, in which, owing to extraordinary atrophy of the bone-marrow, there arises an intense oligocythemia and oligochromemia with but trifling evidence of structural degeneration and nucleation of the red corpuscles. In attempting the antemortem differentiation of aplastic anemia and anemia of the symptomatic variety (which attempt must needs frequently be conjectural), attention should be paid especially to these hematological peculiarities of the first-named disease: relatively low color index; absence of erythroblasts of both types—normoblasts and megaloblasts; scarcity of cells showing stroma defects and anomalies of shape and size, and extreme lymphocytic leucopenia. It is also helpful to remember that aplastic anemia is prone to affect young women, is commonly associated with severe hemorrhagic phenomena, and, arising from no apparent cause, pursues a fatal course of short duration, unbroken by periods of remission.

Splenic anemia, a rare and somewhat questionable clinical entity, causes a blood deterioration in no wise different from that accompanying an ordinary symptomatic anemia with leucopenia. But in splenic anemia there is an idiopathic splenomegaly without enlargement of the lymphatic glands, and, in the later stages of the disease, biliary hepatic cirrhosis, jaundice, and ascites supervene, to complete the symptom group sometimes spoken of as Banti's disease. Disturbances due to severe anemia and to the pressure of an enormous spleen are generally conspicuous, and the disease is likely to develop insidiously, drags along for several years from bad to worse, and eventually kills.

Leukemia is easily distinguished from secondary anemia by means of its distinctive blood picture, as well as by certain objective symptoms. In the myelogenous form the combination of a high leucocyte count and excessive numbers of myelocytes (*myelemia*) is conclusive, and in such cases the spleen is generally enormous; in the lymphatic variety the detection of a high absolute and relative lymphocytosis (*lymphemia*) is equally convincing, and here it is the rule to find great hyperplasia of the lymphatic glands.

Chloroma may account for an anemia identical with that of the secondary type, and it may also produce a blood picture closely comparable to that of lymphatic leukemia. In the former instance the low hemoglobin and erythrocyte values are accompanied by a relative increase in the number of lymphocytes, though the total leucocyte

count does not exceed normal, while in the latter the blood shows great anemia with decided lymphemia. This being the case, one must recognize chloroma not by any distinctive blood formula, but by the chloromatous symptom-complex, made up of exophthalmos, deafness, severe orbital pain, elastic swellings in the orbital and temporal regions, and the formation of metastatic "green tumors" in the periosteal structures.

In *Hodgkin's disease,* which in time gives rise to high-grade secondary anemia, the existence of a progressive glandular hyperplasia in the neck, axilla, and groin is conclusive evidence, apart from the presence of pressure symptoms, irregular fever, cutaneous bronzing, asthenia, and extraordinary emaciation, which together spell this malignant affection.

PROGNOSIS.—It is scarcely necessary to state that the prognosis in a given case of secondary anemia must depend upon the circumstances prevailing in the instance in question, the character, duration, and curability of the primary lesion being the decisive determining points of the forecast. The outlook in gastric cancer, for example, is very different from that in simple inanition or in one of the milder infectious diseases. On the whole, secondary anemia is a symptom that is promptly amenable to intelligent treatment, in strong contrast to which fact is the utter hopelessness of accomplishing a permanent cure in those deadly primary diseases of the blood, pernicious anemia and the leukemias.

TREATMENT.—Iron and **arsenic, nutritious food,** and **correct hygiene** will cure secondary anemia—provided that the essential cause of this symptom be removed. It is just as important to attend to a mass of bleeding piles or to treat an albuminuria in an anemic person as it is to prescribe hematinics, and, by the same token, it is equally important to outline a regimen in which an **out-of-door life, ample sleep,** and **rational personal hygiene** are items of strict observance.

The percentage of hemoglobin in infancy is below 55 at birth and not rising above 70 during the period properly so-called of infancy. The number of red corpuscles varies between 5,500,000 and 6,000,000. This low hemoglobin percentage is presumably due to an insufficient supply of iron in its food and the lack of sufficient reserve of iron in the liver at birth. It is probable that true chlorosis never occurs in infants as a disease, but it is a fact that the chlorotic type of blood is very common at this age. **Iron** is, therefore, specially indicated, but it is difficult to get infants to take iron by the mouth, and it is very liable, moreover, to disturb the digestion. It is desirable, therefore, to give it some other way, and infants take it subcutaneously without injury. A very serviceable form for subcutaneous use is the aqueous solution of the citrate. This can be put up in pearls, each one containing a single dose, in which form it remains sterile indefinitely. It is absolutely non-irritating, and never causes abscess or induration if properly given, though it is somewhat painful. A glass syringe with an asbestos packing, which can be sterilized, and platinum needle that will not corrode with the iron. The average dose during infancy is three-quarters of a grain every other day. He has used this treatment in a number of cases in different types of anemia and with pretty satisfactory results, even in the severe cases. In the mild cases the improvement was very rapid, and the writer's experience leads him to recommend the use of iron in this way. The results are more marked and more quickly obtained than by oral administration, and it is much less liable to disturb digestion. It is especially indicated in severe cases of secondary anemia

with digestive disorder and in those of a sclerotic type. J. L. Morse (Jour. Amer. Med. Assoc., July, 1910).

A chlorotic type of anemia is observed in infants, in which there are pallor, digestive, circulatory, and nervous symptoms and a marked loss of hemoglobin, with a normal number of red cells. The internal organs are normal; there are anemic murmurs in the heart and vessels of the neck. The child is apathetic, quiet, has enlarged glands and sleeps poorly. This condition results when only milk is used, or when it is continued too long. The treatment is improved **diet,** and **iron** is administered in large doses. M. de Biehler (Arch. de Méd. des Enf., Mar., 1913).

A study of the action of **iron** in anemia led the writer to conclude that **iron** in proper doses elicits in a few days a stormy reaction in the bone marrow, which throws quantities of young elements into the blood. In 10 cases of anemia with gastric ulcer, no benefit was evident under iron until large doses were given, and then the hemoglobin ran up rapidly from 37 to 82 and then to 100 per cent., and the reds to 5,024,000. Nägeli (Schweizer. med. Woch., July 29, 1920).

The form of iron to be administered, it is almost needless to state, should be readily absorbable, and unlikely either to upset digestion or to constipate. The **carbonate of iron**, in the pill suggested by Blaud, meets these requirements as well as any other preparation, and has the prestige of a long and dependable clinical usage. Excessive dosage is to be avoided, since the use of 6 or 8 grains a day will accomplish just as satisfactory results as a much larger amount, and will not tend to disturb the stomach or to constipate. **Ferratin** is a meritorious chalybeate, and is, if anything, even less astringent than Blaud's

pill. Of the other iron preparations sometimes chosen for the same reason, the phosphate, lactate, and citrate all enjoy considerable vogue.

The headache of anemia is due chiefly to the deficiency of hemoglobin, and consequent tendency to edema, with the simultaneous starving of the meninges. It is usually frontal, but may be vertical. In certain individuals of lymphatic type, subject to anemia, chilblains, and cold extremities, there may be a deficiency of calcium salts in the blood, and the administration of the calcium salts may be of great service in relieving the headaches of such patients. The lactate should be given in doses of 15 to 20 grains, three times a day. The headaches of the morning after copious libations have been ascribed to a lack of calcium salts in the blood, these having been precipitated by the organic acids contained in the wine.

This headache may be very quickly removed by a dose of 20 to 30 grains of calcium lactate shaken up with a little water. Wilfrid Harris (Practitioner, July, 1906).

There has been distinct progress in the treatment of anemia. The first of these is the method of **direct transfusion** introduced by Crile, whose experiments and results the author considers a brilliant illustration of the value of vivisection to humanity. The second is the use of **colonic irrigations** in pernicious anemia, as recommended by Herter, and successfully employed by Dittmar and Hollis. Herter's discovery that special putrefactive processes in the intestines are due to the prevalence of anaërobic bacteria, particularly the *Bacillus capsulatus aërogenes,* and the parallelism of their presence with the symptoms of the disease suggested this treatment by injections, which the writer considers a valuable therapeutic advance. The third point touched on in his paper is the establishment of the clinical value of **inorganic iron** in the treatment of ane-

mia. Ingested iron, like the carbo-hydrates, is converted into inter-mediate organic compounds and en-ters into the reserve iron stored up in the body, which is normally in excess of the needs of the system. S. J. Meltzer (Jour. Amer. Med. Assoc., Aug. 24, 1907).

Employing the hemoglobin con-tents as an index of the degree of secondary anemia, as well as an actual erythrocyte count, the writers found that the hypodermic use of the **citrate of iron** in the secondary ane-mia of tuberculosis permitted them to control the anemia with almost mathematical precision, and that it actually in no single instance failed to improve the quality of the blood to at least some degree in the 256 cases in which they had employed it. Over 70 per cent. of these cases were in the advanced and far advanced classes, in which the anemia is a commonly manifested phenomenon. The measure was uniformly success-ful in raising the hemoglobin stand-ard to normal in all cases in which the patient might be considered to be doing well, or in which the status quo was seemingly maintained.

It is not necessary to use a larger dose of citrate of iron than 0.05 Gm. Others who have used larger doses have observed sudden vomiting to follow its administration. The tech-nique of the method is to employ the ordinary hypodermic syringe and needle, selecting the buttock as the least inconvenient site of injection, and giving an injection daily until the result is obtained. E. S. Bullock and L. S. Peters (Jour. Amer. Med. Assoc., Oct. 28, 1911).

The writer employed numerous proportions of iron for many years, but in the majority of cases, the re-sults obtained were less favorable than those given by the use of other remedies. **Foods rich in iron,** that is available through digestion, are pref-erable. Whenever the cause of the anemia present can be ascertained the treatment is governed by such data. In those cases not the result

of advancing cardiac, **renal,** hepatic disease, or carcinoma, excellent re-sults follow the use of **readily digested foods, meat juices;** and special attention to the gastric intes-tinal tract. The administration of **red bone marrow** showed in 60 cases of anemia that the red blood cor-puscles, and the hemoglobin were more rapidly increased by this method, together with the fact that the patients were always fed liberally of **green fruit** and **vegetables,** than by any other. Napoleon Boston (Buffalo Med. Jour., June, 1917).

Arsenic is of indispensable value as an adjunct to iron in dealing with anemia, particularly those forms dis-tinguished by relatively excessive oligo-cythemia, as in those severe instances consequent to infectious and malignant processes. The time-honored **Fowler's solution** answers well in the majority of cases, but where an idiosyncrasy exists toward this preparation, as it frequently does, or where it is imperative to stimulate hemogenesis very rapidly, **atoxyl** (sodium anilarsenate) will prove the better form of arsenic. It should always be given hypodermically, in doses of from ½ grain to 2 grains, on alternate days, until the patient has received about 20 grains, after which the drug is discontinued for a week, and then readministered according to the plan originally followed. Given in this manner, one need not fear that lamentable complication, optic neuritis, which has been produced by the ill-advised use of atoxyl. Or **arsacetin** (sodium acetyl arsanilate) may be used, in the same dose and by the same method advised for atoxyl, if it is thought best to employ an even less toxic preparation of arsenic. While useful, manganese, phosphorus, red bone-marrow, hemoglobin, oxygen, and the cacodylates are in no sense adequate

substitutes for iron and arsenic in the treatment of anemic conditions.

Hypodermic medication with **iron** and **arsenic**, together with **strychnine** and the **hypophosphites**, offers a prompt and powerful reconstructive adjunct to the pure air, good food, and sensible hygiene that are essentials in pretuberculous conditions. The **green ammoniated iron citrate** can be introduced into the system, without danger, in doses of from ¾ to 1½ grains, while **sodium arsenate** is given in doses of from 1/60 to 1/30 grain. The injections of solutions of these drugs are given deeply into the muscles of the buttocks or back. Only slight pain attends the procedure, and a general feeling of well-being follows the treatment. A full dose of the iron within five minutes causes a feeling of tension in the head, tingling sensations, and a flushing of the face. Doses larger than 1½ grains may cause nausea or vomiting. B. R. Shurly (Jour. Amer. Med. Assoc., June 16, 1907).

Sufficient is known to justify more than a suspicion that William Hunter was correct in believing that pernicious or infective anemia should be laid at the door of mouth infection. The writer's own experience tends to confirm this belief, particularly in 2 recent cases of pernicious anemia. In 1 patient rigid examination failed to reveal any focus of infection save the mouth, which showed a bad glossitis and pyorrheal abscesses about all the few remaining teeth. After the administration of 5200 c.c. (5½ quarts) of blood by **citrate transfusion** at intervals, the use of **salvarsan** intravenously, the administration of **hydrochloric acid** and good food and rest, only very temporary improvement resulted. When all of the infected teeth were removed, the patient made such rapid and marked improvement that he had now resumed a laborious occupation with the appearance of health and a blood exhibit approximating the normal. M. L. Graves (Trans. So. Med. Assoc.; N. Y. Med. Jour., Jan. 12, 1918).

The anemic subject should eat plentifully of **nutritious, and,** it must be insisted, **palatable, food**—red meats, strong broths, eggs, butter, cream, fruits, and ferruginous vegetables like spinach, asparagus, lentils, and cauliflower. If the appetite flags it may be advisable to whip it up with a glass of **stout** or of **mild claret** at mealtime, or by the use of the **bitter tonics,** the amount of food at the same time being intelligently restricted. Indigestion, if not forestalled by a rational dietary, must be combated by such useful remedies as **pepsin** and **hydrochloric acid, pancreatin** and **diastase, pawpaw, charcoal,** and **bismuth.** It is most necessary for the patient to have a free bowel movement each day, to insure which, if other measures fail, it is good practice to resort to **cascara sagrada, phenolphthalein,** singly or combined with **aloin, strychnine,** and **belladonna,** and supplemented by a dram or two of **Carlsbad salts** dissolved in a tumblerful of hot water, to be slowly sipped each morning directly on arising. Intestinal fermentation, the bane of so many anemics, is best treated dietetically (eggs are notorious offenders), by **intestinal irrigation,** by the administration of cultures of the **lactic acid bacillus,** and by the use of **B-naphthol, salol, bismuth salicylate, phenol,** and similar antifermentative drugs. In patients with troublesome nervous symptoms **strontium bromide** and the **valerianates of iron, quinine,** and **zinc** are helpful adjuncts to the therapeusis suggested above.

In anemia due to autointoxication from the gastrointestinal tract, as

often occurs in chlorosis: 1. Favor gastric functions by **proper diet.** 2. Secure regular bowel movements by **laxatives.** 3. Begin the use of iron, giving following pill: **Subcarbonate of iron,** 0.10 Gm. (1½ grains) ; **powdered aloes,** 0.02 Gm. (⅓ grain) ; **extract of rhubarb,** 0.05 Gm. (¾ grain); 2 pills before meals. Huchard and Fiessinger (Revue de thérap., March 15, 1910).

The writer advises the daily use of **green vegetables,** not only for the anemic and dyspeptic, but for the healthy as well. **Chlorophyll** has been given as such to the anemic, but doubtless cannot replace the fresh vegetables. Maillart (Corres.-Blatt f. Schweizer Aerzte, June 3, 1916).

In a comprehensive study of the blood regeneration following simple anemia in the dog, the writers found that Blaud's pills are inert when added to various **diets** which do not favor rapid blood regeneration. In an animal bled till the pigment was reduced to a level of 40 per cent. below normal, followed by the institution of a **meat diet,** the pigment level normalized within 4 weeks. With milk diet the 40 per cent. level persisted. A fasting animal with access to water could reproduce the hemoglobin, showing that the body could reorganize its elements into hemoglobin. **Spinach** was found to return the level of hemoglobin to normal and keep it there. Milk gave the minimum regeneration. Cooked **liver** and cooked **beef heart** produced the best regeneration. Hooper, Robscheit and Whipple (Amer. Jour. Physiol., Sept. 1920).

[It should be borne in mind that experiments in animals, particularly where the morbid process is produced artificially, do not always portray faithfully a blood disorder in man.—ED.]

In the management of acute anemias of grave character (*i.e.,* posthemorrhagic variety) the **direct transfusion of an homologous blood,** may prove to be a life-saving expedient. The technique and other details of this operation are discussed elsewhere in this work. (See VENESECTION AND TRANSFUSION.)

In 8 instances of **blood transfusion** because of simple secondary anemia or because of anemia and malnutrition, the blood was usually obtained from the father or mother after physical fitness was demonstrated by the absence of agglutination and hemolysis. The blood was withdrawn from a vein of the donor into a syringe and injected directly into the vein of the infant. The syringe was washed out with sterile salt solution before being refilled with blood. Satisfactory results were obtained in all but 1 case, although the children were all under two years of age, both in the digestive capacity and general health. C. G. Kerley (Amer. Jour. of Obstet., lxxvi, 713, 1917).

The writer advocates **transfusion** before operation in severe secondary anemias, on the basis of a case of uterine fibromyomata complicated by severe uterine hemorrhage of 6 weeks' duration. For 6 days following the patient's admission her general condition became much worse, the red blood count falling to 845,000 per cubic millimeter, when 600 c.c. of citrated blood were transfused into the median basilic vein. The effect was most decided. Three days later the temperature was normal, the vomiting had ceased, and control over the bladder and rectum had returned. The red cells had risen to 3,485,000, and the white cells had fallen to 29,000 per cubic millimeter. Fifteen days later a subtotal hysterectomy was performed. This was followed by uninterrupted recovery. H. Williamson (Proc. Royal Soc. Med., London, xiii, Sect. Gynec. and Obstet., 149, 1920).

Hydrotherapy and **general massage** must be regarded as most useful aids to the drug treatment of anemia, and such measures, when sanely carried out, will do much to promote adequate excretion and secretion, to

maintain a healthy balance of the blood and lymph streams, and to stimulate oxygen and carbon dioxide interchange. A regimen of **fresh air, sunshine,** and **gentle exercise** is of great value, added to the foregoing hygienic measures, and in this connection it is interesting to recall Gardinhhi's statement, recently voiced by Pope, that the presence of sunlight promotes the absorption of iron from the liver, where this metal, after ingestion, is presumably stored in no inconsiderable quantity.

Very small doses of **salvarsan**—0.05 or 0.075 Gm. (¾ to 1⅛ grain)—is a simple and harmless method of giving arsenic. It was extremely effectual in 50 cases, increasing the weight, improving the blood-picture ·and subjective symptoms in all forms of secondary anemia and mild tuberculosis. From 10 to 15 injections were given, the course being repeated after an interval of a few weeks. Kall (Münch. med. Woch., July 7, 1914).

The **X-rays** in large doses destroy the bone marrow, but in small doses enhance its activity. This explains their beneficial effects in severe anemia observed by the writers with very mild exposures, the rays being filtered through 2 or 4 mm. of aluminum. Vaquez and Aubertin (Arch. des mal. du Coeur, Sept., 1915).

Case of von *Jaksch's anemia* in a child of 18 months on whom the writer performed a **splenectomy,** with good results. Red count, 2,700,000; hemoglobin, 45 per cent.; white cells, 12,000; polynuclears, 47 per cent.; normoblasts and megaloblasts were present. A spleen weighing 230 grams, showing a high grade meloidization, was removed May 11, 1915. Three weeks after the operation the red blood count had risen to 4,500,-000, and the hemoglobin to 60. Pool (Annals of Surg., lxiii, 122, 1916).

In von *Jaksch's anemia* the most prominent feature of the symptom-complex is an enlarged spleen, but the other hematopoietic organs must be involved more or less extensively. The treatment has been unsatisfactory in the majority of cases; in 6 cases, however, treated by **splenectomy** the operation was followed by immediate clinical improvement. Frequently they tend to recover, when almost any treatment may be followed by improvement, while others progress to a fatal issue in spite of any treatment. R. G. Stillman (Amer. Jour. Med. Sci., Feb., 1917).

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J. C. Da Costa, Jr.

AND

Henry D. Jump,

Philadelphia.

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ANENCEPHALY. —This monstrosity is characterized by the absence in part or *in toto* of the brain and spinal cord. In most instances, however, the central nervous system is poorly developed, and the child if borne alive is idiotic in proportion as the brain is deficiently developed. A curious and suggestive feature of this condition is that the adrenal cortex is poorly, if at all, developed. Thus, Apert (La Presse Méd., Oct. 28, 1911) states that this fact was first observed by Morgagni. It has been verified in hundreds of cases of anencephaly, pseudoencephaly, cyclopia and in a limited number of cases of hydrocephaly and microcephaly.

In a case reported by F. B. Talbot (Med. Rec., Sept. 11, 1915) the child was blind, deaf, and apparently idiotic, and its metabolism was extremely low. An operation for the possible relief of the blindness showed that the hemispheres were absent and replaced by cerebrospinal fluid. When the spinal cord is alone developed more or less, the movements are mainly reflex, as stated by Bronwer (Nederl. Tijdsch. voor Gyn., Aug. 16, 1913). He enumerates among the features to be ascertained the existence of syphilis, through the Wassermann test. Alfred Gordon (Med. Rec., Jan. 31, 1914) failed to obtain a positive reaction in the father of a case observed by him, but a history of alco-

holism and of conception during a period-
ical spree.

> The writer was able to diagnos-
> ticate a case of anencephaly before
> birth by means of X-ray. This in-
> dicates the value of radiography
> where Cesarean section is to be per-
> formed, this operation being rendered
> unnecessary where the presence of a
> monster is ascertained. J. T. Case
> (Surg., Gynec. and Obstet., Mar.,
> 1917).   S.

ANESIN. See CHLORETONE.

ANESTHESIA. —While the various
anesthetics: Ether, chloroform, etc., are
considered under their respective head-
ings, many features of special interest can
only be brought out by considering these
agents collectively. Hence the present
section.

CHOICE OF ANESTHETICS.—A. S.
McCormick (Summit Co. Med. Soc., Ak-
ron, Ohio, Feb. 1, 1916) states that while
the anesthetics most generally used are
ether, nitrous oxide, chloroform, ethyl
chloride, their relative merits are as
follows:

Ethyl Chloride: The anesthetic and
toxic stages are so close that it is too
dangerous. Death rate, 1-2550 (1905-11).
Its chief use is to begin anesthesia, for
which it is quick and efficacious, but even
then it is too dangerous.

Chloroform: Its many good points are
outweighed by its one bad—that of being
a dangerous heart depressant. Death rate,
1-2000. In warm climates it is safer, the
rate being 1-8000.

Nitrous Oxide: Alone it is a dangerous
anesthetic. It has recently been exten-
sively used, combined with oxygen. While
safer than the original method, it is losing
ground as too dangerous. The death rate,
1905-11, was 1-657. Crile states that in
unskilled hands it is the most dangerous
of all anesthetics.

Ether: Admitted by all as safe, it is,
beyond question, the safest and best of all
anesthetics. Figures vary as to death,
those of Wharton being 1-16,000 cases;
Baldwin, 1-50,000; Rovsing (Denmark),
1-56,000; that is, death really caused by
ether. At the Mayo Hospital ether was

given 49,037 times in 13 years (1900-12)
without causing death.

Ether-oxygen is still safer and better.
Less ether is required; the anesthesia is
quiet and just deep enough; the oxygen
counteracts the otherwise ether irritation;
the patient's color is better than under any
other anesthetic.

Referring to experience in the late
war, the writer notes that **ether** was
used most extensively on account of
its convenience and comparative
safety. Scotch surgeons in the Brit-
ish service clung to **chloroform**, how-
ever, and their results were excellent.
Ether-oxygen was a favorite method
in serious cases, the oxygen from a
low pressure tank being sent through
a Shipway apparatus to provide a
warmed ether vapor. When compact,
portable American gas-oxygen de-
vices became available, the **nitrous
oxide-oxygen** technique won the favor
of surgeons of all the allied armies.
It gave promise of obviating to a
great extent postoperative pneumonia.
Warmed ether vapor was found quite
superior to the drop method in every
respect. Morphine was withheld from
those in severe shock, as it lowered
resistance in a marked degree; even
¼ grain (0.016 Gm.) of morphine
may invite disaster in the presence of
shock or hemorrhage. Nitrous oxide-
oxygen proved the anesthetic of
choice in this condition. It was found
very dangerous to alter the position
of patients on the table after anes-
thesia had continued for more than ½
hour. Five c.c. (1½ drams) of chlo-
roform as a single dose proved to be
an invaluable method for transient
anesthesia or analgesia for minor
procedures. Spinal anesthesia, used
to some extent in base hospitals, was
found to be especially dangerous in
all patients showing a low hemoglobin
index. W. S. Sykes (Trans. Amer.
Assoc. of Anesthet.; Jour. Amer.
Med. Assoc., Aug. 9, 1919).

Chloroform given by the **closed method**
with rebreathing is, according to Gwath-
mey, one of the safest of all anesthetics.
It is agreeable, efficient, and easily stopped
upon the appearance of danger signals.

Late chloroform poisoning does not occur and complications are rare.

Ether given by the **vapor method** is much safer, more agreeable, more efficient, is easily controllable, simpler to administer, is not accompanied by loss of resistance against pus organisms, and not so frequently followed by complications as ether administered by the open drop method; the latter is unscientific. It has won unmerited favor within the past few years because of its apparent simplicity of administration and its supposed safety. It should be replaced by the simpler and safer vapor method.

As a simple substitute for intratracheal anesthesia and the complicated apparatus required for it, the writer recommends **vapor anesthesia** with the Hitz bottle and foot-bellows, the latter being cheaper, more portable, and as efficient as an electric motor blower. The anesthetist soon learns to control the volume of air with the bellows, and the Hitz bottle is so made that any portion of the pumped air may be forced through the anesthetic agent. A cylinder of oxygen is attached for emergency use or to augment the atmospheric air current from time to time if cyanosis is observed. Use of a chloroform-ether mixture is advocated. For induction the nitrous oxide-oxygen-ether sequence is preferred. For young children, the essence of orange-ether sequence is best, but for maintenance a mixture of chloroform and ether is advised. The proportion in most cases is, roughly, chloroform 1 part and ether 2 parts, but this is varied according to the type of patient, and the chloroform is increased in the mixture when difficulty in maintenance is anticipated. W. H. Long (Amer. Jour. Surg., xxxiii, Anes. Supp., 77, 1919).

Oil-ether colonic anesthesia should be used whenever the anesthetist is in the way, or whenever the element of fear dominates the patient. The obese alcoholic is the best subject for this special agent.

Nitrous oxide gas should never be used alone, but always with oxygen. Preliminary medication of some kind should be used in all surgical cases unless contraindicated (Gwathmey).

Minor surgical operations or those on the extremities are best done under **nitrous oxide oxygen**. For all operations requiring complete muscular relaxation, especially in abdominal surgery, the **nitrous oxide ether** sequence is the method of choice. **Chloroform** is too dangerous for general use, but it may more safely be used **in combination with ether. Intratracheal insufflation** is of value for thoracic operations. **Rectal anesthesia with ether** in 5 per cent. oily solution is suited to operations on the head and neck combined with local anesthesia. **Morphine** and atropine injections are to be used systematically. A. R. Egana (Semana Med., Apr. 29, 1920).

Addition of a small amount of **magnesium sulphate** to the usual hypodermic of **morphine** greatly increases the value of the hypodermic. The author thus converts colonic anesthesia into **synergistic colonic analgesia,** *i.e.,* he obtains complete brain block by using much smaller amounts of ether than heretofore and adding to it the effects of the combined morphine and magnesium sulphate. Furthermore, with 3 hypodermic injections, each of $\frac{1}{8}$ grain (0.008 Gm.) of morphine and 2 c.c. ($\frac{1}{2}$ dram) of magnesium sulphate, supplemented by **nitrous oxide** and **oxygen** (the latter in high percentage) an analgesic state with unconsciousness and complete relaxation is secured which entirely eliminates the necessity for ether.

Morphine, whenever indicated, may be given in a 25 per cent. sterilized solution of chemically pure magnesium sulphate. This increases the value of the morphine from 50 to 100 per cent. J. T. Gwathmey (Jour. Amer. Med. Assoc., lxxvi, 222, 1921).

PRELIMINARY NARCOTICS.—
Blumfeld (Proc. Roy. Soc. Med., viii, Sect. Anes., 15, 1915) held that the giving of narcotics preliminary to the anesthetic has great value in some cases, while in others it should not be used. As a routine

measure these drugs should not be employed with the single exception of **atropine**. He had never seen or heard of any ill-effects from it so used. Scopolamine and morphine seem risky drugs to prescribe indiscriminately. After the hypodermic the patient should be undisturbed and should not walk to the operating room. The main advantages of preliminary narcotics are: (1) a quiet induction; (2) less anesthetic used; (3) diminished after-effects. Atropine contributes to the first and second.

Hewitt (Proc. Roy. Soc. Med., viii, Sect. Anes., 15, 1915) had found preliminary narcotics valuable when used with discriminating care. The anesthetist should be familiar with his patient's condition. Careful notes of 266 cases in which he had used morphine, atropine, and scopolamine in different combinations show that **atropine** is a very valuable anesthetic, preventing undue secretion and causing little after-vomiting. It has no contraindications. **Scopolamine** is to be feared, $\frac{1}{100}$ grain (0.00065 Gm.) having caused in an elderly man profound narcotization. The injections were made $\frac{3}{4}$ hour beforehand. **Morphine** is strongly contraindicated in certain cases: nose, throat, and tongue operations with hemorrhage in which it is highly important that the reflexes should return rapidly.

Boyle (Proc. Roy. Soc. Med., viii, Sect. Anes., 15, 1915) urged the advantage of the patient's seeing the anesthetist a day or 2 before operation, so that he might have a better knowledge of the patient's condition. He had witnessed the use of **morphine, atropine,** and **scopolamine** in a war hospital. It added greatly to the comfort of both the soldiers and surgeons, the only drawback being the extreme thirst and dryness of the throat.

MISCELLANEOUS FACTORS—

Fright.—Badly frightened patients, according to Scholz (Beit. z. klin. Chir., June, 1914), are inclined to tachycardia, false angina pectoris, polyuria, glycosuria, nervous diarrhea, transient numbness, angioneurotic edema, shallow, rapid breathing, with occasional deep breaths, tremor, pallor and dryness of the mouth. Carbon dioxide seems to be a special product of extreme dread. The blood-pressure in

such patients suffered a constant and regular decline as the ether or chloroform was administered, until consciousness was entirely lost; the patient is exposed to various dangerous reflex processes, especially to reflex syncope from irritation by the anesthetic of the terminals of the trigeminus in the nose, the reflex action from this involving the vagus terminals in the heart and the respiration center in the medulla. This can be warded off by cocainizing the nose. The fatalities as general anesthesia is just commenced are undoubtedly due to this dangerous reflex. The whole secret is to tranquilize the patient, avoid anything suggesting force, and refrain from beginning to operate too early. Persons with marked dread of the operation are exposed to peculiar dangers at the first whiffs of the anesthetic..

Breathing Test to Ascertain Condition of Heart Muscle.—General anesthesia is particularly dangerous to persons suffering from myocardial changes, a condition which does not permit of ready recognition. W. A. Schtange (Roussky Vratch, Jan. 18, 1914) found that while a healthy person can suspend breathing from 30 to 40 seconds, owing to the vigor of the heart muscle, in persons with weak hearts the time is shortened to 20 or even 10 seconds. The patient, seated in a chair, is told to take a moderately deep inspiration, and, with the mouth closed, to hold his breath as long as he can. The shorter the time the patient can suspend breathing, the greater the danger of an anesthetic, the latter being contraindicated if the time is less than 20 seconds.

Pre-anesthetic Diet.—Opie and Alford (Jour. Amer. Med. Assoc., Mar. 21, 1914), in a series of experiments upon animals, using chloroform as an anesthetic, and employing fats and meats as well as carbohydrates as foodstuffs, found animals which received carbohydrates survived; whereas all of those which received meat and fat died. The use of fats increased the susceptibility of the liver to necrosis of chloroform, while a carbohydrate diet seemed to protect the liver from this disaster.

Postoperative Analgesia.—Postoperative analgesia recommended by B. Van Hoosen (Boston Med. and Surg. Jour., clxxx, 556,

1919), to secure painless convalescence for surgical patients: **Morphine,** ¹⁄₃₂ grain (0.002 Gm.), and **scopolamine,** ¹⁄₂₀₀ grain (0.0003 Gm.), are given every 4 hours by hypodermic injection for 24, 36 and, in very painful cases, 48 hours after operation. In 452 cases so treated the effects were found to be most beneficial to both patient and nurses. The method greatly decreases complicating stomach symptoms, shortens convalescence, prevents dread of future operations, and facilitates the work of the nurse. For the first 2 days after operations, the patients had not only marked analgesia but also some amnesia.

Trendelenburg Position as Source of Danger.—In MacCardie's opinion (Proceed. Roy. Soc. of Med., Sect. of Anes., Apr., 1914), anesthetics have frequently been blamed for complications which are really induced by the Trendelenburg posture, especially when the angle of inclination has exceeded 45 degrees. It not only promotes copious venous hemorrhage, and embarrasses pulmonary ventilation, but also puts an additional strain on the heart. Likewise it seems to be an important factor in the occurrence of post-operative pneumonia and bronchitis; and Zweifel holds it occasionally responsible for post-operative intestinal obstruction, surgical emphysema, apoplexy and acute dilatation of the stomach.

Shock During General Anesthesia.—F. C. Mann (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 16, 1917) states that the most common of its causes is free hemorrhage. All persons do not react similarly to loss of blood. Trauma to the viscera is a common cause when accompanied by loss of circulatory fluid in the traumatized areas. Excessive nerve irritation is probably of rarer occurrence than clinical reports indicate. In cases of fractures and trauma to large areas of fat, pulmonary fat embolism might act as cause. The ductless glands, particularly the adrenals, are sometimes factors, possibly as primary active agents or owing to the low blood-pressure and the changes incident to the condition itself. Deep etherization may produce most of the symptoms of shock.

A. Bowlby (Lancet, Jan. 17, 1920) notes that where anesthesia must be used shortly after recovery from the more urgent symptoms of shock, ether, though unlikely to cause pulmonary conditions or vomiting when warmed, produces a dangerous and prolonged lowering of blood-pressure. The most satisfactory results are obtained with **nitrous oxide** and **oxygen** combined with **local infiltration** of the region of the incision, particularly in abdominal operations.

Post-anesthetic Intoxication.—During anesthesia the reserve of glycogen in the system is rapidly consumed, and if this supply were replenished by the administration of **glucose** to the patient, the possible harmful consequences of anesthesia could be in a large measure avoided. Chauvin and Oeconomos (Presse méd., Dec. 18, 1912) administer it as prophylactic in the following form:

R *Glucose* .... ℥v (150 Gm.).
  Tincture of nux
    vomica .... ♏viij (0.5 c.c.).
  Tincture of cinna-
    mon .... ♏xlv (3 Gm.).
  Water, enough to
    make .... ℥x (300 c.c.).
M.

Where post-anesthetic intoxication is already established, glucose should be freely administered by mouth, rectum, and even intravenous injection. As in diabetic coma, alkalies should also be given.

Post-anesthetic Vomiting.—Renton (Brit. Med. Jour,. Dec. 6, 1913) advises to **raise the head of the** patient's **bed** 12 inches, on blocks, leaving it in this position (Fowler's) 24 to 36 hours.

E. M. Barker (Brit. Med. Jour., Jan. 10, 1914) recommends the application after anesthesia, of **eau de Cologne** on a mask immediately, and allow patient to inhale this for half an hour after being placed in bed, the Cologne-water being renewed as required.

Vomiting.—D'Arcy Power (Pract., July, 1920) states that when vomiting is not very severe, **sips of hot water** may be given. In more persistent cases 15 grains (1 Gm.) of **sodium bicarbonate** may be dissolved in a tumblerful of hot water; the patient vomits it directly, but the sickness afterwards subsides. In very severe cases give nothing by mouth, but administer a

sedative enema, consisting of **potassium bromide** and **chloral hydrate,** of each 20 grains (1.3 Gm.), and **mucilage of starch,** 2 ounces (60 c.c.). When vomiting has been unduly prolonged it is sometimes a good plan to feed the patient **solid food** rather than to restrict him to "slops."

C. J. Larkey (Jour. Med. Soc. of N. J., xiv, 8, 1916) attributes post-anesthetic vomiting to the *acidosis* (*q. v.* this volume) which follows the physicochemical combination of the anesthetic with the lipoids, a process followed in hernia by increased acidity of the cell content and increased capacity for water. To prevent acidosis the preoperative preparation should include a regular diet with plenty of **starchy foods** up till noon of the day before operation, then a supper of **cereals, milk** with **albumin, water,** and **sugar.** If *acetone* is present in the urine the **proteids** should be **cut down** and the carbohydrates increased. Water containing **calcium** is useful, while the administration of **sodium bicarbonate and lactose,** 1 dram (4 Gm.) of each every 4 hours for 48 hours before operation is advisable. Following operation the patient is given a 5 per cent. solution of **anhydrous dextrose** by the drip method per rectum, using 250 c.c. (8 ounces).

Untoward Effects of Adrenalin. —Levy (Brit. Med. Jour., Sept. 14, 1912) found that **adrenalin** exerted a very pronounced cardiac effect in chloroformed subjects. Within a few seconds, injection of 5 minims (0.3 c.c.) of the 1:1000 solution caused pulse acceleration and a raised tension; it became more rapid and was less readily felt owing to diminished excursion. It may, or may not, be perceptibly irregular at the wrist; a few temporary pauses were noted, and then the heart suddenly ceased beating; the pupils dilated widely, and intense pallor supervened. Respiratory phenomena followed; a few deep breaths were taken, and the respirations ceased also. The writer concludes that it is *unsafe to inject adrenalin into the veins or vascular tissues* of a patient lightly under the influence of chloroform. It may be safely injected just previous to the induction, however, or into a patient fully under chloroform, or into a patient anesthetized to any degree with ether. In the case of light chloroform anesthesia the risk taken is unjustifiable.

[The injection of adrenalin into the veins is dangerous under *any* circumstance. S.]

Depree (Brit. Med. Jour., Apr. 26, 1913) observed sudden death from cardiac arrest after the injection of 5 minims (0.3 c.c.) of a 1:1000 solution of adrenalin in the nose of a patient who had been anesthetized with chloroform. At the time of the injection anesthesia was light, the corneal reflex being brisk, and no more chloroform was given. All attempts to resuscitate the heart failed.

NARCOANESTHESIA.—This term is used by Henry Beates (N. Y. Med. Jour., Jan. 13, 1917) to identify a method which is asserted to have secured unconsciousness and perfect freedom from pain and exert a minimum of injurious effects. About 2½ or 3 hours before the operation, the patient receives a hypodermic injection of ⅕₀ grain (0.0013 Gm.) of **scopolamine hydrobromide** and ⅙ grain (0.01 Gm.) of **morphine.** One-half hour later, a second injection is administered and an hour later a third, which may or may not contain morphine, as the susceptibility of the patient is more or less apparent. At the time of the third injection an enema of 2 fluidounces (60 c.c) each of **whisky** and **spiritus ætheris compositus** is given. By the time the hour for the operation has arrived, the patient is, as a rule, in a condition of complete narcoanesthesia. The face is more or less flushed. Occasionally there is moderate pallor. The respirations resemble those of profound sleep and, because of the morphine and the susceptibility of the patient to its action, there may be a retardation of the respiratory rate to as low as 10 or 8 to the minute. There has been no material disturbance of the renal functions observed in any case; this suggests that even with the coexistence of renal degenerative lesions narcoanesthesia is safe. Operations upon the biliary tract, herniæ, appendicectomies, pelvic operations of major type, such as hysterectomy, plastic work in the pelvic canal, operations upon the kidneys and rectum, constitute a group that may be most admirably subjected to narcoanesthesia and performed with the leisure

necessary for thorough surgery. One important precaution is the patient must never be left alone, or without an intelligent attendant, as there is danger of strangulation. Dr. Wayne Babcock suggests the placing of a wisp of cotton to the nostril, which serves as an indicator of the ingress and egress of breath, thus preventing a mistake in considering the convulsive movements of strangulation for those of respiration. The patient sleeps from 3 to 7 hours after the operation and awakes often without any discomfort except slight dryness of the nose and throat.

LOCAL ANESTHESIA.—According to R. E. Farr (Amer. Jour. Obstet., lxxx, 653, 1919), the method of choice in local anesthesia is infiltration when it does not interfere with the anatomical relation of the tissues, but in some cases, hernia for example, nerve blocking is recommended. Abolition of the reflexes of the abdominal wall is the ideal in abdominal operations under local anesthesia. Vertical retraction and great care in the handling of the tissues are important points.

Eggleston and Hatcher (Jour. Am. Med. Assoc., Oct. 25, 1919) assert that acute intoxication in man from local anesthetics is far more common than is indicated by the number of recorded cases. In over 300 experiments in cats it was found that when large fractions of the minimal fatal doses are injected intravenously at intervals of from 15 to 20 minutes, or when relatively dilute solutions of the drugs are injected slowly and nearly continuously, the several drugs can be divided into 2 groups as regards rate of elimination. Group 1 includes alypin, apothesin, beta-eucaine, nirvanin, procaine (novocaine), stovaine, and tropacocaine, all of which are rapidly eliminated, so that several times the minimal fatal dose can be injected in the ways just mentioned in periods of 1 or 2 hours without causing death. Group 2 includes cocaine and holocaine, which are much less rapidly eliminated and therefore cause death in much smaller total doses when given as described. The elimination of all the local anesthetics is accomplished almost entirely by their destruction in the liver.

Epinephrin and artificial respiration should prove effective as a resuscitative measure in many cases of acute poisoning in man. To diminish the likelihood of intoxication from the subcutaneous injection of local anesthetics in man, epinephrin should always be added to their solution.

Novocaine (procaine) being the safest anesthetic known, a more dangerous drug should not be used, according to Farr (Trans. Amer. Med. Assoc.; Med. Rec., May 15, 1920). Many children are in a bad condition following the use of a general anesthetic, and the nature of the anesthetic often decides the issue. A child can be restrained on an arm table set at right angles to the operating table. The feet are attached by bandages to the operating table, and the nurse holds the arms above the elbow. As a rule the child needs restraint only while the anesthetic is being given. One should always be prepared to reinforce the local anesthesia with general anesthesia; but it is rarely necessary. Farr refers to a series of 129 cases of children operated under local anesthesia and in only 9 of whom there was any pain; when this occurs it is due to an error in technique.

COMPARATIVE MERITS OF VARIOUS LOCAL ANESTHETICS.—G. MacGowan (Calif. State Jour. of Med., Jan., 1916) holds that a local anesthetic to be valuable must not of itself be a cause of pain, either before its action is established or after it has ceased. None of the drugs are used pure, but all need to be dissolved in fluids isotonic with the juices that bathe the body cells, such as a 0.9 per cent. solution of common salt. Cocaine, the first local anesthetic to be discovered, has been abandoned because of its disadvantages except in eye and nasal surgery, and sometimes in urethral operations where the newer and safer anesthetics are inactive. Tropacocaine is the ideal agent for spinal anesthesia. Beta-eucaine does not differ widely from cocaine; as a protoplasmic poison, it produces the same symptoms, but the dose required is greater. It is slightly less powerful as a local anesthetic, does not diffuse so well, and is more irritating. Its solutions are stable and can be sterilized by boiling. Acoin is a dangerous poison, and is decomposed readily by alkalies. Holocaine anesthetizes the eye without

dilating the pupil, producing dryness of the cornea, or preventing bleeding. **Chloretone** or **anesol** is very irritating. **Orthoform, anesthesin, subcutin, propesin, and zykloform** are all slightly soluble powders with anesthetic properties when brought in contact with exposed nerve filaments or endings. They are used upon the skin in dusting powders or salves, in the rectum or vagina as suppositories or salves, and are also useful in the nose, throat, and intestinal tract, especially the stomach. The most efficient of the group is **anesthesin,** over which the others possess no advantages. **Stovaine** has been recommended for spinal anesthesia, but is irritating and painful for infiltration anesthesia. In a 1 per cent. solution it is useful as a local anesthetic when used by instillation for an instrumental examination of the urethra and bladder. **Alypin** is a close relative of stovaine, is readily soluble in watery solutions, is less active and more irritating than cocaine when used hypodermically, and its toxic symptoms are similar to those of the latter. **Novocaine** is but feebly poisonous, its watery solutions up to 10 per cent. are not irritating; it may be sterilized and resterilized without marked effect upon its anesthetic properties, which are greater than those of any other drug used for local anesthesia, when combined with suprarenine, with the exception of cocaine. It can be applied pure to the cornea and to freshly denuded surfaces without causing pain or subsequent edema. For infiltration anesthesia isotonic solutions of ½, 1, 2, and 4 per cent. are the most useful; greater concentrations are not necessary and should not be used, even though it is only feebly toxic. **Hydrochloride of quinine and urea** in watery solutions of from 0.25 to 1 per cent. causes the formation of a fibrinous exudate in tissues infiltrated with it, which delays the healing of wounds. Tetanus has been observed after this salt has been used. Its one valuable quality is the length of time its anesthetic effects last, sometimes for many days, on account of which it may be used to inhibit pain in intense and persistently localized *neuritis,* and in blocking the sensation of itching in circumscribed and chronically thickened patches of *eczema.*

Benzyl alcohol was found by the writer to be a fairly efficient anesthetic for intact mucous membranes, greatly surpassing procaine, ranking about with alypin and betaeucaine, and somewhat weaker than holocaine or cocaine. Its action is not as lasting as that of ·cocaine, and even 1 per cent. solutions produce much smarting. Sollmann (Jour. Pharm. and Exper. Therap., July, 1919).

ANESTHESIA ACIDOSIS.—In gathering data to indicate the character of the operative risk, it has been customary for a long time, as stated by H. Morriss (Jour. Amer. Med. Assoc., May 12, 1917), to employ uranalysis, blood counts, hemoglobin determinations and estimations of the arterial tension. It seems advisable often to add to these the determination of what has been called the "alkali reserve"; for postoperative nausea and vomiting, menacing convalescence, may depend on an acidosis for which the anesthetic is responsible. Under normal circumstances the acid-base equilibrium is remarkably stable. The· mechanism involved in the maintenance of the equilibrium comprises: (1) the elimination of carbon dioxide by the lungs; (2) the excretion of acid salts by the kidneys and sweat glands; (3) the presence of "buffer" substances in the blood which include the bicarbonates, phosphates, and probably proteins; (4) the production of ammonia at the expense of urea, and (5) the influence of the barometric pressure (oxygen tension) to which the individual is accustomed, a factor as yet imperfectly understood. It has been demonstrated that the lungs take a leading part in the regulation of the acidbase equilibrium of our bodies. The carbon dioxide which the lungs excrete has acid properties; when in the blood it is neutralized through combination with alkali. The excess of available alkali is termed the alkali reserve. This may be estimated indirectly by the determination of the carbon dioxide in the alveolar air, or of the capacity of the blood plasma to combine with carbon dioxide.

In anesthesia there results a compensated *acidosis* in from 30 to 85 per cent. and an uncompensated acidosis in from 15 to 20 per cent. of cases.

The protection of the patient from acidosis rests in limiting suboxidation and in supplying the body with alkali. The acids are usually neutralized as they are formed by sodium bicarbonate, ammonia, and less easily mobilized bases, such as calcium and magnesium. The symptoms vary from headache, nausea and vomiting, gas pains and mental dullness, to coma and death. The following factors influence uncompensated acidosis: extreme age, impaired kidney function, exhausting diseases, prolonged sepsis, duration and depth of anesthesia, hemorrhage, and preoperative fasting. Shock is always associated with uncompensated acidosis. A patient showing before operation a low bicarbonate content should be given the benefit of alkalinization with **sodium bicarbonate,** though further studies may show the use of **magnesium** and **calcium** to be equally important. Too much alkali may do harm; therefore, a second analysis 2 hours after alkalinization should be made, to ascertain whether the desired result has been attained. S. P. Reimann (Trans. Amer. Assoc. of Anesthet.; Jour. Amer. Med. Assoc., Aug. 2, 1919).

ANESTHESIN. — Anesthesin is,
chemically, ethyl para-aminobenzoate [C_6-$H_4.NH_2.COOC_2H_5$]. It occurs as a white, odorless, and tasteless powder, almost insoluble in cold water, with difficulty soluble in hot water, sparingly soluble in fatty oils (2 to 3 per cent.) and in dilute glycerin, easily soluble in alcohol, ether, chloroform, benzene, and acetone. It melts at 90° to 91° C. Though decomposed by prolonged boiling, it can be rendered sterile without deterioration when dissolved in oils. Alkalies and alkaline carbonates are incompatible with it, removing the ethyl group to form alcohol and setting free para-aminobenzoic acid.

PHYSIOLOGICAL ACTION.—The most conspicuous feature of anesthesin is its local anesthetic property. The drug differs radically from cocaine in that it is but very feebly toxic and is insoluble in water. The low toxic power was shown in the experiments of Binz, who administered 0.6 Gm. (10 grains) of the drug in 20 c.c. of oil by stomach tube; on the next day the animal was in good health, with urine normal. The dose required to kill was found to be 1.15 Gm. (18 grains) per kilo of animal, the symptoms produced being paralysis, gradual loss of sensibility in the hind limbs, and dyspnea terminating in asphyxia. The drug was also administered intravenously in dogs and intraperitoneally in guinea-pigs, with similar results indicative of a low degree of toxicity.

The intoxication produced by anesthesin is in some ways comparable to that of acetphenetidin; massive doses lead to the formation of methemoglobin, with consequent methemoglobinuria.

Anesthesin placed upon the tongue produces a feeling of numbness in two to three minutes. By virtue of the insolubility of this substance, its anesthetic action is more strictly localized than that of cocaine. It is also feebler, but is more enduring. It is said to exert no action on the vessels at the site of application, causing neither vasoconstriction nor vasodilation. Over orthoform it has the advantages of being more stable and practically non-irritating.

THERAPEUTIC USES. — Internally, anesthesin, as first demonstrated by von Noorden, is useful in conditions of **gastric hyperesthesia,** including **nervous dyspepsia** and **gastric ulcer.** The dose is 0.2 to 0.5 Gm. (3 to 7½ grains) ten to fifteen minutes after the ingestion of food. In **laryngeal tuberculosis** an insufflation of anesthesin has been found by Courtade to arrest the severe pain and, therefore, the dysphagia for nearly forty-eight hours. Earp found it very useful in very painful bleeding external **hemorrhoids.** The bowels were moved freely by enemas, hot applications were used freely, and the following ointment was applied twice daily:

℞ *Anesthesin* .... 15 grs. (1 Gm.).
Ergotin .... 1 dr. (4 Gm.).
Ichthyol .... 30 mins. (2 Gm.).
Lanolin .... 3 drs. (12 Gm.).
Petroleum ..to make 1 oz. (31 Gm.).

Earp also found anesthesin useful in perineal **eczema** which had not yielded to other measures. S.

ANEURISM. —DEFINITION.—

An abnormal circumscribed blood-tumor containing a cavity communicating with an artery. An aneurism consists of a sac, neck, and contents. The contents include liquid blood, coagula, and laminated fibrin. Aneurisms vary in size from that of a millet seed to that of a child's head. In order of frequency aneurisms involve the thoracic aorta, popliteal artery, femoral artery, abdominal aorta, subclavian artery, innominate artery, axillary artery, iliac artery, and the cerebral and pulmonary arteries.

VARIETIES.—Congenital. — Congenital aneurisms are extremely rare, but they have been reported involving the abdominal aorta and ductus Botalli. A rare congenital deficiency of the elastic elements of the walls of the arteries may be the cause of multiple aneurisms, especially involving the smaller arteries of the body.

Idiopathic. — Idiopathic aneurisms are those arising without obvious traumatic injury to the vessel wall. They are usually dependent upon disease of the artery, and constitute most of the aneurisms involving the great vessels of the trunk, and the smaller aneurisms of the brain and other viscera.

Traumatic.—Traumatic aneurisms are those resulting from mechanical injuries sustained by the arterial wall, either in the form of a contusion, incision, or laceration.

Hernial.—Hernial aneurisms are usually small traumatic aneurisms produced by the bulging of the inner tunic through the divided outer layers of the arterial wall.

True.—True aneurisms are those having walls formed by the normal coats of an artery. It is rare, however, to find an aneurismal sac in which intima, media, and adventitia can all be demonstrated.

False.—False aneurisms are those in which the sac is formed by tissues other than those derived from the wall of the artery. They follow arterial incisions or ruptures, but even with these false sacs the endothelium proliferates from the intima of the artery into the sac and finally tends to line it.

Diffuse.—Diffuse aneurisms are false aneurisms resulting from an extensive extravasation of blood from an open artery. As a rule, they are due to traumatism, but they also result from the spontaneous rupture of a diseased artery.

Dissecting. — Dissecting aneurisms are those in which the aneurismal sac lies between the coats of the artery. As a rule, they have two mouths, the blood entering through one opening, separating the layers of the arterial walls, and then, at some distance, recommunicating by a second opening with the arterial stream. These occur most frequently in the abdominal aorta and may produce a very extensive separation of the arterial coats.

Embolic.—Embolic aneurisms are those resulting from the lodgment of emboli. By some they are attributed to the laceration of the walls of the small vessels by calcareous embolic particles. It is evident that they may also result from degenerative or inflammatory changes of the arterial wall, secondary to the lodgment of the embolus.

Embolomycotic aneurisms develop during the course of endocarditis and occasionally during some of the acute infectious diseases, which form a distinct group by themselves, differing in pathogenesis, clinical course, and prognosis from those developing secondary

to chronic arterial changes. They have been recognized since 1851. They may develop in one of three ways. Most commonly they follow an endarteritis associated with lodgment of infected emboli at the bifurcation of arteries. A few cases have been reported which developed during the course of infectious diseases unaccompanied by endocardial changes. The possibility of traumatic origin is also supported by the observation of Ponfick and Thoma of calcified emboli in the arterial wall and projecting into the aneurism. Clinically, embolomycotic aneurisms differ from those following chronic arterial changes: (1) in developing at an earlier age; (2) in frequently being multiple, acute and chronic forms often occurring in the same individual; (3) in the frequent involvement of visceral arteries, and (4) in the tendency to remain small. A number of cases have been reported in which no satisfactory explanation is given of the cause. About one-fourth of the cases observed developed during the third decade of life, and about one-fourth during the second.

They are much more frequent in males, although the authors have been unable to demonstrate the reasons for this satisfactorily. They have collected, including their own cases, 96 aneurisms of this class occurring in 65 patients, they frequently being multiple, and report 3 cases observed by themselves. The largest proportion of these aneurisms occurred in the superior mesenteric and cerebral arteries, and in the aorta, which is in marked contrast to the distribution of the ordinary type of chronic aneurisms, which rarely occur in the superior mesenteric or cerebral arteries. There is nothing characteristic in the symptoms, and they are not often suspected until fatal abdominal or cerebral hemorrhage occurs. Bacteria have been found within the wall of the aneurism, showing the bacteriological relationship between the vegetations on the heart valves and the clot in the aneurism. The forms are usually the streptococcus and staphylococcus, though other species have been reported. In 2 of the author's cases, examinations revealed the pneumococcus. This infection of the aneurisms complicates any operation, the patients being usually in a critical condition and not enduring surgery well. Dean Lewis and V. L. Schrager (Jour. Amer. Med. Assoc., Nov. 27, 1909).

Miliary. — Miliary aneurisms are very minute aneurisms most frequently observed in the brain or lungs. They involve small- or medium- sized arteries and often occur in great numbers.

Fusiform or Ectatic. — In these forms the weakened arterial walls yield in every direction, forming a fusiform, or, rarely, a somewhat cylindrical, enlargement. The three coats of the artery may be demonstrated in the sac; usually there is little clot present, and there may be few symptoms, unless through weakness of a part of the wall a sacculated aneurism follows. The walls of the fusiform aneurism may be thicker than that of the adjacent artery.

Sacculated.—Sacculated aneurisms are due to the bulging of one side of an artery. The elastic and muscular layers of the artery are not found in the walls of the sac.

ETIOLOGY. — Aneurisms result from conditions weakening the arterial wall and increasing the blood-pressure.

Race. — The Anglo-Saxon race is most frequently affected; the English more than the American, a condition attributed to the greater consumption of alcohol in England. Aneurism is rare in the Asiatic races and in Italy. It is three times as prevalent in the American negro as in the white race.

Age.—Aneurism is most frequent between the ages of 30 and 50, a period when degenerative changes in the ar-

teries are especially found in those engaged in laborious physical work.

Sex.—Men are affected ten times as frequently as women, excepting the carotid and dissecting forms of aneurism, which occur more frequently in women. The more laborious occupations of men and their greater tendency to dissipation and excess explain the influence of sex.

Soldiers, sailors, athletes, cab drivers, furnace men, and others engaged in violent, but intermittent exercise are especially predisposed to aneurism. It is eleven times more frequent in the English army than in the civilian, and is much more frequent in soldiers than in sailors, a condition attributed to the pressure and strain from poorly fitting clothing and heavy accoutrements. Cab drivers, apparently from the pull upon the arms, are especially susceptible to thoracic aneurism.

Vessels at the point of flexion and extension, such as the popliteal and iliacs, or under greater strain, such as those of the right arm rather than the left, are more frequently involved. Occasionally symmetrical aneurisms, as double popliteal aneurisms, occur.

Those conditions that produce a weakening of the arterial wall, especially all the causes of arteriosclerosis and atheroma, are important predisposing causes to aneurism. These include syphilis, alcoholism, rheumatism, gout, and the action of mineral poisons like lead.

Arterial disease appears to be rare, almost unknown, in animals. Syphilis, being probably peculiar to man, is by this observation placed more firmly in the list of etiological factors. Arterial disease in children under 6 years, even in those who are victims of congenital syphilis, is practically unknown. In those from 6 to 15 years it is rare. It is found in the initial stage most com-

monly between the ages of 30 and 40 years. The teratological factor, though an undeterminable one, is of great importance. Arterial disease seems to be attributable to syphilis in about 32 per cent., to tuberculosis in about 16 per cent. The facts presented go to show that the colored race is affected about four times more frequently than the white.

General arteriosclerosis seems to be not commonly found with aneurism, and its presence may be considered as evidence against the probable development of aneurism.

Staining with selective stains and treating with a chemical which digests tissue show the elastic tissue to be free of histological alterations, suggesting that this tissue undergoes physical or molecular rather than histological change. C. N. B. Camac (Amer. Jour. Med. Sci., May, 1905).

The influence of rheumatism is one of great importance, especially in young patients. The writer, working with Rénon, has recently published some important observations relative to this subject. According to the cases collected by this author, the average age is from 10 to 16 when the patients have usually had several attacks of acute rheumatism. Repetition of the disease is regarded as an essential factor. The appearance of aneurism is preceded for some time by the signs of aortic incompetence and hypertrophy of the heart. After a period of considerable latency, the symptoms and signs of aneurism appear rapidly. They are dyspnea, especially marked after effort, and characterized by forced inspiration without actual oppression. After a short time this dyspnea becomes permanent, though occasionally varied by pseudoasthmatic crises, sometimes attacks of pain resembling angina pectoris. The attacks usually appear during the first sleep. The patient retires to rest in his ordinary condition, but suddenly awakes in great agony, complaining of a feeling of constriction in front of the chest, air hunger, desire to cry out, and violent inspiratory efforts are made. The crisis may last

from a quarter to one hour, and then gradually disappear. Occasionally the crises are entirely painful without respiratory trouble. Considerable intervals may elapse between them, for in one case quoted by the author they numbered 2 or 3 during the year; in others they are more frequent, occurring once a month, or even daily. The diagnosis is confirmed by the rapid appearance of physical signs. These aneurisms, as a rule, affect the upper right costal area, and do not differ from those usually observed in other cases. Aortic aneurism in young rheumatic subjects may develop fully in the course of a few weeks, sometimes in succeeding stages corresponding to the rheumatic crisis. After each crisis there may be temporary improvement, due to retrocession of the tumor. This improvement is reversed by a fresh crisis of articular inflammation. The condition is, therefore, progressive, and there is little hope of obliteration taking place in the sac. Prognosis is usually fatal, death often occurring suddenly either from hemorrhage or angina pectoris. Feytaud (Thèse de Paris, 1906).

The writer obtained a history of syphilis in over 77 per cent. of 34 cases of aortic aneurism at the Helsingfors Hospital since 1900. In the 10 tested for the Wassermann reaction, it was positive in 90 per cent. The shortest interval since infection was 7 years, the longest 35. The youngest patient was 30 at the time of his death, the oldest 70. In 9 cases rupture of the aneurism was the cause of death, and in 13, interference with the action of the heart. In all but 2 cases the aneurism was in the thoracic aorta. Sjoblom (Finska Läkare Handl., lviii, No. 5, 1916).

Definite evidences of the rather commonly syphilitic nature of aneurism detected. The writer found *spirochaeta pallida* clustered in foci in several cases of aneurism of the thoracic or abdominal aorta. Y. Manouélian (Bull. de la Soc. Méd. des Hôp., May 28, 1920).

Only 5 of the author's 29 patients with aortic aneurism had a history excluding the possibility of syphilis. The outcome was not known in 8 patients, but 9 were still living after intervals of from 16 months to 12 years. Syphilis plus alcoholism is a particularly dangerous combination. Martinet (Presse méd., Oct. 16, 1920).

Cardiac hypertrophy, plethora, and renal disease are also factors. Experimentally, aneurism may be produced by the repeated introduction of adrenalin into the circulating stream.

PATHOLOGY.—Idiopathic aneurisms develop in an area of atheroma, in the situation of an old scar, the point of lodgment of an embolus, or other weak area in the arterial wall. All forms of aneurism are lined by endothelium, excepting the fusiform aneurisms; the media of the artery does not constitute a layer of the abnormal sac. This means that the normal muscular and elastic coats are absent, and that the vasa vasorum upon which the arterial wall depends for its nourishment is lacking. The sacs of all saccular aneurisms thus tend to be weak while blood-pressure causes them gradually to distend.

In the fusiform aneurism all the layers of the arterial walls may remain and the wall of the sac may be thicker than that of the normal artery, the intima being thickened by atheroma, the adventitia by the deposit of fibrous tissue, while the middle coat is thinned. As the inner coats of an artery constitute not less than three-fourths of the thickness of its wall, containing the elastic and muscular layers, and also the vasorum supplying the walls with nourishment, the thinning, absence, or damage to these structures means a weak and poorly resilient wall for the aneurismal sac.

In sacculated aneurisms there is usually a progressive deposit of layers of fibrin against the wall of the sac, tending to strengthen the walls and to lessen the fluid contents. The lessening of the fluid contents is important, as the pressure on the sac wall varies as the square of the diameter of the cavity which contains the fluid.

At times the blood-clot is deposited in progressive layers until the entire sac is filled, resulting in a spontaneous cure. The blood-clot at the periphery is white, laminated, and fibrous, although rarely organized into the true fibrous tissue, the lack of vasorum preventing vascularization. The aneurism, therefore, may consist of a sac or body, which in the sacculated form may communicate by neck and opening with the artery. The sac is strengthened on the outer side by the deposit of fibrous tissue, an evidence of the reaction and irritation of the tissues against which the aneurism presses.

The sac may contain peripherally white, laminated clot; then a layer of softer, red blood-clot, and finally fluid blood communicating with the blood-stream. In the cylindrical and fusiform aneurisms little or no lining clot may be present.

The size and shape of the sac are modified by adjacent pressure. Rotation of the sac may occur so that in a fusiform aneurismal sac the orifices of the efferent and afferent trunks may lie at the sides or at the equator of the sac, rather than at the poles.

Matas classifies aneurisms by the number of orifices which connect them with the parent artery. These orifices may only be accurately determined after the opening of the sac. Fusiform aneurisms have two distinct orifices; saccular or sacciform aneurisms are those which are connected with the lumen of the parent vessel by a single circular, ovoid, or elongated opening through which the blood flows in and out the sac.

The sac of the aneurism may have many collateral branches corresponding somewhat with the branches normally given off by the segment of the arterial wall forming the aneurism. These collaterals may be functional or impervious and containing thrombi. The perianeurismal circulation may be very important in maintaining the collateral circulation after operation upon the sac. An aneurism influences the blood-stream, absorbing the cardiac wave, so that the pulse distal to the sac is delayed and weakened. To compensate for this the heart may hypertrophy and anastomotic channels form.

The aneurism may so press upon the main vessels as to completely interrupt the circulation beyond the sac. The adjacent tissues are variously affected. Bone is eroded and progressively destroyed by the continuous pressure, cartilage being much more resistant than bone.

Nerves are stretched, compressed, and flattened, at times destroyed, giving rise to paresthesia and more rarely paralysis. Adjacent veins may be compressed with the production of cyanosis and edema, and rarely erosion and perforation in the venous channel occur. Mucous canals are compressed and displaced, while fibrous tissue, tendons, and fascia are flattened, stretched, and often incorporated into the sac.

Thrombi may form in tributary vessels, and emboli may result from the dislodgment of clot or fibrin. Cerebral complications, such as hemiplegia, infarcts in the internal organs, and gangrene of the extremities, also occur.

SYMPTOMS.—Aneurismal dilatation may occur suddenly from traumatism or a great increase of intravascular pressure and may be characterized by sharp pain and rapid enlargement along the course of an artery. The sac, however, usually forms slowly and at first without pain or any other symptom.

Case of a woman aged 42 years, attended by remarkable features. The aneurism was eroded and perforated the sternum in two places without ever causing pain or any other pressure symptoms; it presented externally as a tumor, and then disappeared under treatment by iodide of potassium, the skin rupturing without letting out any blood. This series of events was repeated several times in the course of seven years. Death occurred from the sudden bursting of the aneurism as the patient lifted a pitcher of water. R. C. Cabot (Amer. Jour. Med. Sci., April, 1900).

The diagnosis of aortic aneurism still remains in obscure cases a difficult one, and even the X-ray examination may be misleading. Attention called to the frequency with which, in aneurism of the arch, the left supraclavicular groove is obliterated or even bulges, and the left external jugular is obviously fuller than the right. The anatomical reason lies simply in the compression of the left innominate vein as a result of the dilated arch. A mediastinal tumor may have the same effect, but dilatation in cases of aortic insufficiency is apparently seldom sufficient to effect compression. Dorendorff (Deut. med. Woch., Nov. 31, 1902).

Pain is one of the earliest and most constant symptoms of aortic aneurism. It was the first and most severe symptoms in about half of the author's cases. It is possible that it should be absent, though there may be dyspnea, cough, and cyanosis, and though the sac may perforate the chest wall or erode the spine. The most common situation for the pain is in the region of the heart itself, radiating to the neck, the shoulder, and back, and down the left arm or both arms. In some cases the abdominal pain is severe. Several distinct varieties of pain may be recognized in this disease: 1. Attacks of true angina, having paroxysms of pain of maximum intensity, with radiation to the arm. 2. Sharp neuralgic pain due to pressure on the nerves, perhaps extending along the course of the nerves, and associated with herpes when the descending thoracic aorta is implicated. It is similar in character to that which is caused by the pressure of pelvic tumors, and by disease of the vertebræ, and it may be paroxysmal in character. 3. Pain of a dull, boring character which is present when the chest wall or the spine is eroded by the aneurismal sac. This is the form of aneurismal pain which is most enduring and most severe. It is due to tension and stretching of fibrous and bony structures rather than to pressure upon nerve cords. 4. Pain referred to the nerves of the arms or the skin in the precordial region or to the pectoral or sternomastoid muscles.

One object of the writer's paper was to narrate types of cases in which attacks of angina pectoris customarily precede the appearance of the aneurism for months or years. The paroxysms may not be in the least suggestive of aneurism, but they are associated with early structural changes in the wall of the aorta. In sclerosis of the aorta pain is not necessarily a symptom, the author having observed this fact in syphilitic patients. With lesions of arteries the pain may be the most intense, this being frequently observed in embolism, thrombosis, and the ligation of vessels. W. Osler (Med. Chronicle, May, 1906).

With the exception of the rare cases in which there is trouble with swallowing, the early symptoms of aneurism, manifested by pressure, are usually either pain or disturbance with the respiratory apparatus. The latter may come either from pressure on the air passages or from pressure on the recurrent laryngeal nerve. The symptoms frequently simulate those of heart

disease, and their true meaning is learned partly by not finding a cardiac condition that will explain the symptoms, and partly by looking for and finding evidence of an aneurism.

The picture of aortic aneurism in its earlier stages is not uniform, but varies widely with the position and size of the aneurism. There are no pathognomonic signs. Yet a careful physical examination and a careful consideration of the physical signs and symptoms should enable the detection of the existence of an aneurism of the ascending or transverse arch at a very early stage.

An early positive diagnosis of aortic aneurism is obtainable only by the X-ray. Expansile pulsation is not constant. Abnormal dullness is a valuable sign when present. The most constant sign is systolic bruit, which was present in 11 of 19 cases. Tracheal tugging occurred in but 2 cases. The earliest and most constant symptoms were dyspnea and cough. Interference with passage of bismuth capsule the size of a quarter through esophagus was found present in every case tested (by X-rays). This is especially valuable in small aneurisms growing back from the transverse part of the arch, as it shows the esophageal obstruction before dysphagia appears. Lange (Lancet-Clinic, Feb. 19, 1910).

Only 2 phenomena were present in any considerable percentage of the cases, *pain* and *dullness*. The pain may be substernal, vertebral, may extend down either arm or up the side of the neck to the occiput. The pain may be continuous or may occur as typical attacks of angina. Percussion seems to yield earlier information of an intrathoracic growth than any other method of physical examination. Lemann (Amer. Jour. Med. Sci., Aug., 1916).

The writer found 17 cases of aneurism of the splenic artery mentioned in the literature. His own patient complained of dyspnea on exertion and edema. The abdomen was distended and tympanitic, with a definite fluid wave and shifting dullness. The temperature varied from 98° to 103° F. Abdominal paracentesis was performed, the trocar being inserted in the midline about midway between the umbilicus and pubis. After 1200 c.c. of slightly cloudy, reddish fluid had been withdrawn, the flow stopped. At the second puncture, ½ inch lower down, the patient at once experienced a sharp pain in the abdomen, and the needle was withdrawn. Patient collapsed and died in 3 hours. The necropsy showed a ruptured aneurism of the splenic artery, not due to trauma. Garland (Boston Med. and Surg. Jour., Apr. 14, 1921).

The aneurism forms a smooth round or oval enlargement in the course of an artery. It is not sensitive, unless inflamed, is not adherent to the overlying skin, but may be associated with edema and venous congestion of the parts distal to the tumor. The swelling has an expansive pulsation up to the time that a sufficiently thick layer of clot forms within the sac to abolish this sign, so that the symptoms are at times divided into those of the expansile and those of the non-expansile stage. The artery distal to the aneurism gives a retarded and feeble pulse. The expansile pulsation may be less marked and the tumor softer when the parts are elevated. The pulsation is diminished by pressure upon the main artery proximal to the aneurism, and in some cases the sac may then become softer and collapse. On auscultation a systolic or sometimes a double rough murmur or bruit is heard, loudest at the proximal pole. A shadow, emphasized if calcareous deposits are present, may be shown by the fluoroscope or skiagraph.

Subjective symptoms include pain from the stretching and compression of nerves and the arrest of the venous or lymphatic circulation. The pressure and erosion of bone, especially noticed

in aneurisms of the aorta, cause the characteristic boring, so-called osteopathic pains which are usually more severe at night.

In the skull the rushing sound and bruit, headache, and the evidences of cerebral pressure or irritation, such as choked disk, vomiting, dilated pupil, motor and sensory disturbances, and localizing nerve palsies, may be present.

> When an aneurism causes paralysis of the third nerve alone, it is uniformly seated upon the trunk of the internal carotid, between the origins of the anterior and posterior communicating arteries. When the aneurism involves the origin of the posterior cerebral artery, the paralysis of the third nerve is accompanied by paralysis of the corresponding facial. The only subjective symptoms (besides the diplopia) are pains in the head and constant noises upon the same side as the aneurism. These cases always end fatally. Pascheff (Archiv d'ophtal., Oct., 1910).

In the neck the situation of the tumor, expansile pulsation, and the effect upon the distal vessels are characteristic symptoms.

In the chest the recurrent laryngeal nerve frequently is involved with the production of rasping voice, spasm or paralysis of the vocal cord, and brassy cough. Pressure upon the sympathetic may produce unilateral sweating and unilateral contraction or dilatation of the pupil as well as tachycardia. Peripheral neuralgia may result from compression of the intercostals. Compression of the phrenic may cause dyspnea and hiccough, while pressure upon the esophagus may result in dysphagia.

> Although there is no one pathognomonic sign of thoracic aneurism, there are certain symptoms and signs taken together which make its exist-

ence practically certain. The pain, often slight and not complained of except after particular inquiry, is continuous, is situated near and to the left of the vertebral column, and tends to radiate to the shoulder, the left arm, and the neck. Examination of the chest shows no loss of resonance on the left side, but the resonance is not increased as in pneumothorax. At the same time the breath sounds are diminished over the left lung—this being due to partial compression of the left bronchus. The inspiratory sound is shorter over the left side, the first period of inspiration being inaudible and the air then entering with a rush, as though a valve had been opened. On inspection, there is relative immobility of the left side of the chest, or in some cases there may even be definite retraction. If the above signs be present, together with dyspnea on effort, in a patient whose general health is fairly good and who has no sign of malignant disease, the presumption of the existence of aneurism is strong. Inequality of the pupils is often an early symptom. Clément (Lyon méd., March 31, 1907).

In 40 cases of aortic aneurism investigated at the Seamen's Hospital, Greenwich, the blood-pressure on admission was invariably above normal. A difference of 5 or 10 mm. Hg. between the two arms was of little importance, but a marked difference of from 15 to 20 mm. or so was strong evidence of the presence of aneurism. Mackinnon (Brit. Med. Jour., Oct. 4, 1913).

Hemoptysis from perforated aortic aneurism was witnessed by the writer some 15 times owing to tracheal or bronchial perforation, all the cases being necessarily fatal. But with the diagnosis established, hemoptysis may not, however, mean that the aneurism has burst. It may be due to atheroma of the pulmonary vessels, or the aneurism itself, still intact, may cause a perforation into the pulmonary artery. Hampeln (Deut. med. Woch., May 1, 1913).

The various pulmonary lesions caused by or associated with aortic aneurism include collapse, bronchiectasis, chronic pneumonia, and, rarely, localized gangrenous areas around the bronchi. They are apt to resemble pleuritic effusion, malignant disease, cirrhosis, and phthisis very closely. In some cases tuberculosis develops in the lung, which is thus collapsed or affected with chronic pneumonia. Bramwell (Edinburgh Med. Jour., Feb., 1916).

Tracheal tugging is often found in aneurism of the arch of the aorta, and is due to the transmission of the aneurismal pulsations to the left bronchus, and is detected by inclining the head and lifting the larynx and trachea by the finger and thumb caught under the hyoid bone.

Two cases of aortic aneurism were observed by the writer which were mistaken for asthma, owing to absence of tumor, pulsation, thrill and bruit. The diagnosis was made by inspection and confirmed by röntgenograms. S. Solis Cohen (Interstate Med. Jour., Jan., 1912).

Inanition may follow in the rare instances in which the thoracic duct is compressed. In thoracic aneurism the distal vessels show a retarded and reduced pulsation, so that the pulse may be weak or even absent from one wrist.

In examining for aneurism of the aorta, one should carefully percuss the area of dullness of the great vessels, note the conduction of the heart sounds in this area, examine both radial pulses simultaneously, examine for the tracheal tug, note all evidences obtained by inspection or palpation, note carefully all the anatomical relations of the aorta, and ever keep in mind the possibility of aneurism. Arnold (Amer. Jour. Med. Sci., Apr., 1908).

In cases of thoracic aneurism, delay or increased retardation of one of the radial pulses does occur. The same delay may or may not be present in the case of the corresponding carotid pulse. If the idea, based on experimental physics, be correct, that delay of the pulse-wave is only produced as the result of the wave passing through the aneurism, then the phenomenon of delay should be of most important diagnostic aid in the localization of the aneurism. Digital examination is not a reliable test of the presence or absence of delay. The finger may miss the delay when present, and may diagnose it when absent. A more delicate instrument, such as the clinical polygraph, is necessary. Leonard Findlay (Practitioner, Dec., 1909).

In 2 cases observed by the writer, the arteriovenous aneurism became transformed into an arterial form, and this retrogressed spontaneously and totally in 1 case, partially in the other. Chevrier (Presse méd., Dec. 19, 1918).

Rupture is signalized by pain of sudden onset with shock.

Two cases of aneurism of the abdominal aorta apparently of arteriosclerotic origin which ruptured into the duodenum. Marlow and Doubler (American Journal Med. Sci., April, 1918).

Series of cases illustrating the many directions which aortic aneurisms may take in relation to other organs. In 1 case the perforation was external, through the sternum; in 1 it was into the superior vena cava; in 1 it was into the left pleural cavity by way of the diaphragm; in 1 it was retroperitoneal; in 1 it was into the left pleural cavity by way of the left lung; in 2 it was into the left main bronchus; in 1 it was into the left ventricle; and in 1 it was into the pulmonary artery; 6 were therefore aneurisms which sprang from the arch of the aorta. Two were developed from the abdominal aorta. Woolley (Amer. Jour. of Syphilis, Apr., 1917).

As a result, the hemorrhage may escape externally through the skin, into the trachea, or into the alimentary

canal; if into the pericardium there are evidences of acute heart compression; if into the cavity of the thorax, of hematothorax; if into the muscular substance, the formation of a progressively enlarging tumor. The rupture may be immediately fatal, or the patient may live for hours or for days, and repeated or continuous leakage may occur. Rarely does recovery follow after an aneurism of one of the great vessels of the trunk has ruptured, although the patient may survive for days or weeks.

> Case of abdominal aortic aneurism in a man aged 41 years in whom the writer observed several hyperesthetic cutaneous zones, as described by Head. Such zones are segmental regions of the body corresponding to the various viscera, exactly at the sensory innervation of the skin, as described by Sherrington, Starr, Kocher, and Thorburn. Trophic disturbances occur in the skin in disease of the arteries, as, for example, in zoster. The points noted in the study of the present case included the belt-like distribution of the radiations of pain due to the abdominal aneurism, these pains dating many years before the development of the symptoms. E. Cedrangolo (Riforma medica, Mar. 23, 1907).

COURSE.—Aneurisms tend to progressively dilate and finally to rupture. In rare instances an aneurismal sac may remain stationary for many years, finally to again progressively dilate. In a third class spontaneous cure occurs by the coagulation of blood within the sac, which may completely consolidate it, with or without obliteration of the arterial lumen. Any condition which interrupts or retards the circulation through the sac may favor this spontaneous cure. This termination at times is followed by a fatal gangrene from obstruction of the collateral circulation.

Plastic arteritis with thrombosis and obliteration of the artery may also lead to a cure. More frequently the aneurism progresses to rupture. The rupture may occur through the skin, mucous membrane, into a serous or synovial cavity or into the subcutaneous tissues, muscles, or fascial planes.

There may be repeated moderate hemorrhages, one or several large hemorrhages, or a rapid hemorrhage sufficient to cause almost instant death or a progressively increasing hemorrhagic edema from a *leaking aneurism.* This may lead to gangrene.

Suppuration of an aneurism occurs most frequently in the axillary region and usually results from the formation of an abscess adjacent to the sac. The sloughing of the sac wall may be followed by great hemorrhage as the abscess opens. Rarely does a plastic arteritis produce clotting and spontaneous cure.

DIFFERENTIAL DIAGNOSIS. —The expansile pulsation, bruit, and retardation of the distal pulse are fairly characteristic symptoms of aneurism. In a consolidated aneurism, or one in which the sac has been filled by clot, these signs may disappear.

The history and presence of a firm mass in the wall of the blood-vessel are suggestive. Tumors and abscesses lying upon large arteries may pulsate, but the expansile type of pulsation is absent.

When the skin over an aneurism has become inflamed the condition may closely simulate an abscess, so that only by a careful study of the patient is a correct diagnosis finally to be made.

Before the consolidation, compression of the main artery proximal to the aneurism may produce a characteristic

collapse of the sac, a cessation of pulsation, and bruit, changes which cannot be produced in vascular sarcomas and other tumors which may simulate aneurisms.

In aneurisms of the thorax X-ray examinations are often diagnostic.

In suspected aneurisms of the abdominal aorta loss or retardation of the femoral pulse should be especially looked for. The marked pulsation of the undilated aorta in thin persons should not be mistaken for aneurism.

In determining the compressibility of the aneurismal sac the greatest gentleness must be employed. We have observed hemiplegia to promptly follow the examination and the palpation of a carotid aneurism for the dislodgment of particles of contained clot.

TREATMENT.—Dietetic, hygienic, and medicinal measures have been used since antiquity with the object of slowing the circulation and so simulating coagulation that a clot would fill the sac. The ancient method of Valsalva included **absolute physical and mental rest,** a very **limited diet, with the deprivation of fluid,** and repeated venesections continued until the patient was too weak to lift a hand.

The more recent method of Tuffnell's was less severe, although rigorous; it consisted of a reduction in the diet and absolute rest in a horizontal position; 2 ounces of bread and butter are given for breakfast with 2 ounces of milk; 3 ounces of bread and butter with 4 ounces of water or claret for dinner; 2 ounces of bread and butter with 2 ounces of tea for supper. A fat diet has been advised by Powell, and the use of meats has been condemned.

Cure by what was practically the Tufnell treatment. It consisted of as nearly absolute rest as possible, restricted diet for a week and later an ordinary fish diet, no stimulation, and **potassium iodide**, 10 grains three times a day. The dose was quickly and steadily increased so that by the end of the third week 60 grains were being taken three times a day, with no ill effects at any time. As a local application to the swelling, **collodion** was painted all over the surface every night and morning. Instead of continuing his previous downward progress, he commenced to improve from almost the commencement of the treatment, and was discharged apparently cured in six weeks. Young (Lancet, Sept. 22, 1906).

Drugs are employed to reduce the cardiac frequency, to diminish arterial tension, and increase the coagulability of the blood. **Potassium iodide** has been considered to be the most valuable drug. Ten grains three times a day may be increased until 40, 60, or 200 grains three times daily are administered, according to the degree of tolerance. It is especially valuable in syphilitic patients.

In aneurism of the aorta the writer urges antisyphilitic treatment, because syphilis is the fundamental disease in the majority of cases. The best routine procedure is an intravenous injection of 0.2 Gm. (3 grains) **salvarsan** every week until three doses have been given; then, if indicated, it may be repeated in 0.6-Gm. (10 grain) doses a month or 2 apart. In the interim intramuscular injections of **mercury** about twice a week should be given in conjunction with **potassium iodide,** as this treatment often is efficacious and is followed by marked improvement. Selian Neuhof (Amer. Jour. Med. Sci., May, 1916).

To increase the coagulability of the blood in the treatment of saccular aneurisms the subcutaneous injections of **gelatin** were first recommended by Lancereaux and Paulesco.

One or 2 Gm. of purest gelatin are dissolved in 100 c.c. of decinormal salt solution, and sterilized by heating to the boiling point for one-half hour on five successive days. Before use the gelatin is warmed to the temperature of the body and 100 c.c. injected under the abdominal skin every two, three, or four days.

Plea for the use of injections of **gelatin** in aneurism of the aorta. The danger of tetanus is removed if the gelatin is properly sterilized and no disagreeable effects are noticed by the patients. Lancereaux (Revue de thérap., No. 13, 1906).

Case of large traumatic aneurism occupying the lower half of the left popliteal space, and extending downward to a line about 6 inches below the knee-joint. After a prolonged and careful treatment by rest and flexion of the leg, which proved unsuccessful, the author tried repeated subcutaneous injections of sterilized **gelatin** serum. Seven injections were made, the intervals varying from seven to twenty days. The last injection was followed after an interval of about ten days by complete cure. Le Dentu (Bull. et mém. de la soc. de chir. de Paris, No. 10, 1905).

Treatment of 40 cases showed that **potassium iodide** does not reduce the blood-pressure, although it often relieves pain. This can also be obtained by other means, notably by the injection of sterilized solution of **gelatin.** Gelatin does not reduce the blood-pressure, but in Rankin's and personal cases there was very marked relief of pain in almost every instance where such symptom was a prominent feature. Mackinnon (Brit. Med. Jour., Oct. 4, 1913).

Case of aneurism of the ascending portion of the aorta, with distressing symptoms, in which, after intravenous injections of mercury cyanide and gelatin had proved useless, **percussion of the spine** of the seventh cervical vertebra according to Abrams's method (see page 667) was

tried, with signal success. The percussion was practised daily for five minutes. After eight sittings the patient was able to walk five miles without distress, and resumed his work as a baker. R. Houlié (Bull. et mém. de la Soc. de Méd. de Paris, May 8, 1914).

In a certain percentage of cases, according to the writer, it may be possible to overcome the effects of an aneurism and induce a clinical cure by the treatment consisting chiefly in strict **bed rest,** reduction of the diet to 4 **small meals** a day without fluids; only 300 c.c. of fluids are permitted in the 24 hours. **Venesection** may be necessary and **ice** to the region of the aneurism, with local injections of **ergot** around the aneurism and injection of **gelatin** into the buttocks, with **potassium iodide** internally. Maragliano (Gaz. degli ospedali, Jan. 31, 1915).

A medical cure of an aneurism in the middle portion of the right supraclavicular region was obtained by the writer. The man was kept absolutely quiet in bed, on a milk-vegetable diet, without much liquid, and he was given once a week for 20 weeks, a subcutaneous injection in the flank of 60 or 40 c.c. (2 or 1⅓ ounces) of a 2 per cent. solution of **gelatinized serum.** As the Wassermann reaction was positive, mercurial treatment was given at the same time. Improvement was rapid and pronounced. The aneurism subsided to a clinical cure. T. Castellano (Prensa Medica, Feb. 10, 1918).

Several cures have been reported from the use of gelatin, but in other instances undesirable thrombi have formed in the larger veins, while tetanus has followed the use of imperfectly sterilized gelatin. Should the clot which forms in the aneurismal sac soften and be absorbed, the gelatin injections may be repeated with a possibility of good effect.

The internal administration of **calcium chloride** and the subcutaneous

injection of **horse serum** have also been used to increase the coagulability of the blood.

> Case of aortic aneurism in which all the symptoms, except a slight headache, had disappeared as a result of the administration of **calcium chloride** for about two months. The calcium chloride was given three times daily. The aneurism was clearly visible under the X-ray. Ambrose (Jour. Amer. Med. Assoc., Oct. 31, 1908).

Arterial Compression.—The object of this method is to so slow the blood-current within the sac that a coagulum may form. The pressure may be proximal to the aneurism and be carried out by means of a pad, tourniquet, or the pressure of the thumbs of assistants acting in relay. The pressure of the thumb is reinforced by a 6-pound weight, and before the thumb of one assistant is removed that of another is properly placed. Each assistant serves for fifteen or twenty minutes, and the treatment is continued for from twenty-four to seventy-two hours. The method by compression is painful and when instrumental may cause sloughing or gangrene. The digital compression requires many assistants and is troublesome, but not so apt to cause sloughing. The compression occasionally cures, but often if the clot is deposited it is dissipated before organization has occurred.

> Three cases of aneurism followed, 2 for eight years and 1 for four years, in 2 of which permanent cure has resulted from treatment based on a reduction of vascular tension below the normal. The treatment consists in keeping the patient at **rest** in bed and in prescribing a **diet** from which soups containing an excess of fat; meats, especially those cooked rare; game, fish, cheese, salted foods, tea, coffee, spirits, heavy beers, and an excess of wine are eliminated. Tobacco is also forbidden. Drugs, such as **nitroglycerin**

and **sodium nitrite,** were administered. The iodides have been overrated in this connection. In syphilitic aneurisms mercurial injections are dangerous on account of their liability to affect the kidneys, and, as a consequence, to cause increased arterial tension. The **milk diet** in connection with **theobromine,** which assists in eliminating vasoconstrictor poisons, is very helpful in reducing vascular tension. H. Huchard (Jour. des praticiens, Nu. 20, p. 307, 1906).

Forced flexion of the elbow and knee, the part being held by a bandage with the pad at the flexure, has been employed for small aneurisms of the extremities. The position is uncomfortable and the method of little advantage over other methods of compression.

The isolation of a mass of blood within the aneurismal sac by the application of an **Esmarch bandage** below and above the aneurismal sac, while efficient in causing clotting, has led to gangrene of the extremity, and the method has been abandoned. It has been advised that an Esmarch bandage be applied for one and one-half hours and then removed, with continuous light compression of the artery above the aneurism for several days. Apart from the danger of compression, another danger of these methods is in the completeness of the coagulation, which may extend into the collateral vessels and so destroy their function that gangrene follows.

Arterial Ligature.—Ligature of the main artery just above the sac is especially efficient in interrupting the circulation. This is Anel's operation, but was modified by John Hunter, who placed the ligature at a distance above the sac, where he supposed that the arterial walls were healthier. Anel's operation is now preferred to Hunter's.

The most important part of the new surgical work with blood-vessels, especially with aneurism, depends upon the similarity of the serous coat of blood-vessels to the peritoneum. Like the latter, the former throw out lymph for purposes of repair. Irritated surfaces in apposition adhere. Torsion of blood-vessels also causes quick plastic occlusion so that arteries of the third class may be thus treated in place of by ligation. Aneurism treated by **digital pressure,** by the introduction of **coils of wire,** or by **electric needles** causes exudation of lymph from the serous coats, followed by adhesion of apposed surfaces. The new work in suturing blood-vessels depends for its safety upon the prompt plastic repair of the serous coats. Morris (Annals of Surg., July, 1908).

According to the writer, it has been found by English surgeons, contrary to the commonly accepted ideas, that in many cases **simultaneous ligation of vein and artery** may be safer as regards both life and avoidance of gangrene than ligation of the artery alone. H. S. Valentine (Trans. Mo. State Med. Assoc.; Jour. Amer. Med. Assoc., May 1, 1920).

When on account of anatomical conditions the ligature cannot be placed above the sac the method of **distal ligation,** such as Basedow's, in which the main vessel is ligatured, or Wardrop's, in which one or more of the chief branches is secured as by ligation of the right subclavian for aneurism of the innominate artery, may be tried. Rarely are they efficient.

A successful case (the ninth with recovery) of **ligation** of the innominate artery. The patient was a colored man aged 27 suffering from subclavian aneurism; the innominate only was tied with a largest-sized braided silk ligature in a "granny" knot drawn just tightly enough to approximate the vessel walls, but not to crush its coats. The ligature came away 51 days after the operation while the wound was being dressed; the recovery was good practically in 20 days. Burns (Jour. Amer. Med. Assoc., Nov. 14, 1908).

In aneurisms at the root of the thigh the writer resorts to preliminary **elastic compression** with the Esmarch band or by Momburg's method. The blood flow can always be arrested beforehand by passing a strand of catgut beneath the vessels and having an assistant exert moderate upward traction on it. In none of his cases, whether of spontaneous or traumatic aneurism, did gangrene follow **quadruple ligation** of the femoral artery and vein above and below the aneurism, with extirpation of the latter. Even in a large pathological aneurism, with removal of 17 centimeters of the external iliac artery and of the femoral trunk, superficial as well as deep, not the least circulatory difficulty followed—probably in this case because the aneurism was of about 10 years' standing. Much delay in operating on aneurisms, especially in war practice, is inadvisable, for as time passes the aneurism extends, and increasingly firm adhesions with the collateral veins, nerves, and neighboring organs or tissues become established, rendering dissection difficult. Potherat (Presse méd., June 21, 1917).

The late war afforded much experience with traumatic aneurisms. The practical conclusion from discussions and statistics, as expressed by the writers, is that **ligation** and **resection** of the aneurism constitute the safest and best treatment in the majority of cases. Only under exceptionally favorable conditions should end-to-end suture be considered, though this is sometimes the only means to save the limbs. Lenger, Strassen and Vonsken (Arch. Méd. Belges, Aug., 1920).

Dix's Operation.—The artery is exposed and encircled by a strand of silver wire. The ends of the wire are brought through the tissues to one side of the wound, and are twisted over a

split cork until pulsation ceases in the aneurism. Later slight pulsation returns to the sac, and after two or three days the wire is tightened by placing wedges under the loop. About the fifth or sixth day the wire is cut and removed.

Excision of the Sac and Implantation.—The interposition of a segment of an adjacent vein has also been tried, but the procedure has rarely been successful.

Removal or Obliteration of the Sac.—The ancient method of Antyllus, in which the sac was dissected out or opened and packed, has been succeeded by the modern **obliterative method of Matas.** In this operation the patient is anesthetized, a tourniquet applied, the sac is opened by a longitudinal incision, emptied, and the mouth of each vessel is exposed within the sac and sutured from the inside by separate silk or chromicized catgut sutures. The redundant walls of the sac are then so enfolded and sutured as to form a solid pad under the skin. The advantage of this method lies in the fact that the sac is not loosened from the adjacent tissues, and, therefore, there is little risk of injuring adjacent collateral nerves and veins.

> **Matas's method** combines the advantages of ligation and excision, while at the same time it is easier, safer, and may be more conservative. It is suitable both in the fusiform and sacculated types of the disease. After applying a constrictor above the site of the disease, if in a limb, or temporarily ligating the proximal and distal trunks, if the carotid is the vessel at fault, the operator cuts into the sac, thoroughly removes the contained clots, rubs the serosa with gauze, and proceeds to insert sutures. The sutures, preferably catgut, are first applied to the openings of all vessels entering or leaving the sac; then the deeper portions of the

sac are closed by two rows of continuous Lembert sutures. The elastic constrictor is now removed, and if any blood escapes one or two points of suture are inserted to control this. The next step consists in folding the excess of sac wall on itself, and in so doing inverting the edges of the skin wound. The operation thus performed has been very successful, and in some cases of sacculated aneurism the circulation may be re-established through the repaired vessel. Binnie (Jour. Amer. Med. Assoc., June 25, 1904).

Results of **endoaneurismorrhaphy** (the writer's method) in 85 operations by 52 surgeons up to the present date. The legitimate mortality of the operation itself was 2.3 per cent.; of secondary hemorrhage, 2.3 per cent.; of gangrene, 4.6 per cent. Eliminating 3 of the gangrene cases in which there was simultaneous injury and ligation of veins or secondary ligature of an artery, the percentage of this accident is 1.1 only. The total of postoperative deaths from all causes was 7 to 78 recoveries. The percentage of relapses, which occurred only in the reconstructive operations (4 in 13, or 28 per cent.), was only 4.7 per cent. to the total. The author believes that the fundamental principle on which the operation is based, viz., that the endothelial lining of the vascular system which is continued in the aneurismal sac is analogous in its pathological behaviour to the reactions and reparative processes which occur in the endothelial surfaces of the other serosa, such as the peritoneum and the pleura, has been absolutely confirmed by the experience in these 85 cases. They have also disproved Scarpe's law that complete obliteration of the vessel is an essential to the cure, which result is also supported by the facts of the suture and repair of arteries. An important point of the technique is the prophylactic hemostasis, which must be made absolute, and the problem increases in complexity and difficulty the higher the operation, and the writer mentions the method and ap-

pliances for this purpose. Experience demonstrates that in all sacciform aneurisms with a single orifice of communication the closure of this orifice by suture without interfering with the lumen or the capacity of the vessel is to be looked on as obligatory. The indication for the reconstructive operation, however, is fusiform aneurism with separate orifices of entrance and exit. In the vast majority of cases of aneurism of the extremities the simple obliterative procedure proved satisfactory. It gives a cure with less risk to distal parts than ligature or extirpation. Indications in any given case will not be entirely satisfactory until we have a sure clinical proof of the adequacy of the collateral circulation. Korotkow's method of testing the most peripheral blood-pressure may be the proper solution. R. Matas (Jour. Amer. Med. Assoc., Nov. 14, 1908).

The advantages of **Matas's endoaneurismorrhaphy** are as follows: It is more radical in its effects than ligature and extirpation; it is free from risk of injury; it is only exceptionally followed by gangrene; it does not interfere with the collateral circulation; it prevents any danger of injury of a vein, and is applicable to cases in which extirpation is no longer possible. For suture chromicized catgut or fine silk is employed. The method is chiefly indicated in cases in which provisional hemostasis can be carried out and where the aneurismal sac is accessible. Altogether 149 cases have been reported, in 131 of which the lower extremity was affected. Among the last 64 cases there have been no deaths, no recurrences or secondary bleeding, and only one instance of gangrene. Gardner (Gaz. d. Hôp., No. 118, 1910).

A second method is **Matas's conservative endoaneurismorrhaphy,** to be used for sacculated aneurisms opening by a narrow mouth into the main vessel. This opening is sutured from the inside of the sac and the wound reinforced, pleating and suturing the overlying sac. In reconstructive endoaneurismorrhaphy an attempt is made to restore the normal lumen of the artery in a fusiform aneurism. A rubber tube may be temporarily introduced as a guide between the afferent and efferent mouth of the sac, and the walls of the sac so sutured as to restore a canal having the lumen similar to that of the adjacent artery. This line of suture is likewise to be reinforced by pleating and suturing the redundant walls of the sac.

Report of a case of **reconstructive aneurismorrhaphy** in the third part of the axillary artery, the aneurism having been the result of a gunshot wound received 2 years previously. The aneurism and a portion of the axillary artery both above and below were dissected free and Crile artery clamps applied above and below the tumor. The aneurismal sac was then defined up to its point of origin from the artery and opened by a longitudinal incision. At the junction of vessel and sac was a ring of almost cartilaginous density. The sac was cut away so that only a thin rim around the neck was left. With a non-cutting fine needle a continuous suture was introduced, beginning above and finishing below the opening and passing through the arterial wall immediately adjoining the thick ring. Mattress sutures of fine silk were used. A second stronger silk suture was then introduced, the needle traversing the artery wall on either side and returning similarly through the rim of the sac, thus embracing the hard ring and securing apposition of its opposite side. Removal of the clamps revealed no oozing. A fascia lata graft was fixed as a collar about the vessel to diminish the strain on the suture line. Three months later there was no sign of yielding and the brachial pulses were equal. C. J. Marshall (Brit. Med. Jour., i, 379, 1921).

Temporary partial obliteration of the main artery by use of **metallic rings or clips;** Halstead and others have devised rings or clips composed of aluminum or other metal which may be applied to an arterial trunk in such a manner that the lumen in the vessel is reduced or obliterated. By reducing the lumen the current in the artery and sac distal to the ring may be so slowed as to favor curative coagulation, and if properly applied it has been found that these rings are well tolerated by the arterial wall, and have not the same tendency to ulcerate into the lumen of the vessel as a ligature.

The application of a ligature is not feasible in the case of the aorta, for in every case in which a ligature has been employed the patient has died, if not from the immediate danger from the operation, then some days or weeks later from secondary hemorrhage due to the ligature cutting its way through the wall of the artery.

Macewen's Acupuncture. — This method aims to scarify the lining of the sac so that the granulations form upon which the blood may coagulate. One or more long fine-silk needles are thrust into the aneurism so that their points just touch the opposite wall. The pulsatile movements of the sac wall cause the needle-points to scratch the lining of the sac. The needles are left in place some hours, their position then is so changed that as large an area as possible of the lining will be abraded. The method is of very limited value.

Electrolysis increases the efficiency of Macewen's method. Insulated needles are passed and a galvanic current from 20 to 30 milliampères. Needles should be permitted to touch the opposite wall of the sac so as to produce the delicate abrasion as in acupuncture.

Report of 2 cases of thoracic aneurism upon which the Moore-Corradi operation of **wiring with electrolysis** had been performed over 4 years previously. In the first, 17 feet of No. 29 gold "clasp" wire had been used and in the second 22½ feet. Active antisyphilitic treatment was instituted in both patients with great benefit. The best result is obtained when the wire is so introduced as to bring it as much as possible in contact with the wall of the aneurism. This permits the clot produced by the electrolysis to come in contact with vitalized tissue from which it can become organized. W. C. Lusk (Annals of Surg., lxiv, 680, 1916).

Moore's method consists in the use of a delicate wire so tempered as to coil within the sac, where it is permitted to remain permanently. A small, hollow needle is introduced into the sac until the blood flows and from 5 to 20 feet of wire, according to the size of the sac, passed through the needle. The end of the wire is then pushed through the needle or cut close to the skin and made to imbed itself.

The **Moore-Corradi method** consists in passing the current from 20 to 80 milliampères through the coil of wire which has been introduced into the sac. A wire of fine drawn gold is preferred, and from 5 to 20 feet introduced, as in the Moore method. The current is permitted to flow about one hour, negative pole being connected with a pad upon the patient's abdomen or back. The wire is permitted to remain permanently within the sac.

Aneurism of the left subclavian artery in which 20 feet of **gold wire** were introduced into the sac through a hollow needle, and a **galvanic current,** gradually increasing from 1 to 80 milliampères, was employed for about one hundred and ten minutes. The pulsation and size of the tumor temporarily decreased and afterward increased, and

death occurred on the twentieth day after operation, due to exhaustion and pressure thrombosis. Daland (Penna. Med. Jour., Dec., 1903).

Three further cases of sacculated aneurism of the aorta successfully treated by **wiring** and **electrolysis**. The second case was too advanced for anything more than palliation. One of the most important effects is the relief of pain. This is usually immediate. H. A. Hare (Jour. Amer. Med. Assoc., lxxvi, 587, 1921).

These methods have chiefly been employed for aneurisms of the thoracic aorta. Occasionally cures are reported, but failures are frequent and fatal accidents have occurred. It is obvious that even in so-called cures the patient's ultimate condition is not a normal one. Sterilized horsehair, silk, and catgut have also been tried, but with questionable benefit.

A recent addition to the methods of treatment is that of Abrams, which, though qualified by him as palliative, seems to have produced lasting beneficial effects in a large number (40) of his cases. It consists of **repeated concussions over the seventh cervical vertebra,** which are thought by Abrams to cause, through the vasomotor system, contraction of the diseased vascular area. Confirmatory evidence is still too scant to warrant any opinion as to the actual value of this method.

A. Abrams, of San Francisco, claims that the subsidiary center of the vasoconstrictor nerves of the aorta is located in the spinal cord in proximity to the spinous process of the seventh cervical vertebra, and that by stimulation of the center in question by concussion the normal as well as the abnormal aorta may be brought to contraction. Ample evidence is furnished of the latter fact in his work on spondylotherapy. The method, in brief, which he suggests in the treatment of aortic aneurism con-

sists in **concussion of the spinous process of the seventh cervical vertebra.** He deprecates the employment of the conventional vibrating apparatus. The vibratory apparatus which the physician must employ is one giving the percussion stroke. All other motions, such as oscillations, shaking, and friction, interfere with results. In the absence of a suitable apparatus, a pleximeter (a strip of linoleum or thick rubber) and a hammer, to the end of which is fixed a piece of hard rubber, are employed. The pleximeter is applied to the seventh cervical spine and is struck a series of rapid and moderate blows by the hammer. The daily *séances,* according to results, may last from five to fifteen minutes, but during the *séance* the treatment must be interrupted from time to time to avoid irritations of the skin.

The results of Abrams's method are usually immediate, great relief following a few *séances.* When the writer first encountered the monograph of the latter on the subject, he was rather skeptical, although Abrams anticipates such criticism in his book by observing that any merit attached to his method may be obscured by its simplicity.

The writer presents the history of a personal case suffering from aneurism of the thoracic aorta which was treated successfully by the "concussion method" of Abrams. The aneurism had perforated the chest wall. Within one week all the symptoms had disappeared, and fourteen months after the patient's discharge he was as well as when dismissed. L. St. John Hely (Amer. Jour. of Physiol. Therap., July, 1910).

Case of aneurism of the thoracic aorta treated by **Abrams's method.** After the first daily *séance* of concussion, lasting ten minutes, the systolic murmur over the aorta almost disappeared. Three days later the aneurismal dullness measured transversely 2.6 cm. After two more days the aneurism measured 2 cm. and the patient's weight was 123 pounds, an increase of 5 pounds. Two days later there was absolutely no dullness over the site of

the aneurism, the pains in the chest were gone, expectoration was reduced about 50 per cent., but the cough continued with less frequency and severity. After about two months the patient's weight was 135 pounds. He had absolutely no symptom beyond an occasional slight cough. Turnbull (Med. Record, Sept. 9, 1911).

Report of a case of aneurism of the thoracic aorta treated successfully by **Abrams's method.** There was no X-ray verification of the condition in this case, but the physical signs respecting the aneurism and the results of treatment were absolutely positive and unmistakable. Boyd (N. Y. Med. Jour., Oct. 21, 1911).

ARTERIOVENOUS ANEURISM.

—These conditions, termed by Hunter aneurism by anastomosis, are characterized by an arteriovenous fistula. They may be divided into two chief forms:—

(*a*) **Aneurismal varix** is characterized by the direct communication of the artery with the vein. The blood-pressure is much higher in the artery; the arterial flow is forced into the vein, which becomes thickened, dilated, sacculated, and tortuous. The condition is usually due to the incised wound involving the contiguous walls of an artery and vein, and gunshot wounds. Occasionally they result from contusions without external wound, and may even develop spontaneously. In the older days the common cause was phlebotomy. In order of frequency the brachial, femoral, popliteal, carotid, temporal, subclavian, and axillary arteries are involved. Instances are recorded in which the condition has spontaneously occurred in connection with the abdominal and thoracic aorta, and after gunshot wounds of the head a fistula may form between the cavernous sinus and internal carotid artery.

(*b*) **Varicose Aneurism.**—The vein communicates with the artery through the medium of an aneurismal sac. This usually develops from a traumatic aneurism which becomes adherent to an adjacent vein and finally opens into it. Both the artery and the vein may be injured simultaneously and an intermediate blood-clot first form, the sac finally replacing the area occupied by the blood-clot. Such an aneurism may form at the ends of the divided vessels in an amputation stump.

An arteriovenous aneurism with an arterial sac, such as that developed from the erosion of a true aneurism through the wall of an adjacent vein, is rare, and has been classified as a third variety of arteriovenous aneurism.

Symptoms.—A marked pulsation which is communicated widely to the communicating veins is present and usually associated with a loud, whistling bruit. The bruit is both systolic and diastolic. The thrill may be palpable. The interference with the normal circulation in the vein may produce stagnation, local cyanosis, pigmentation, eczema, elephantiasis, muscular atrophy, ulceration, rarely gangrene. The pressure upon the nerves may result in paresthesia or paralysis.

Among 42 cases of traumatic arteriovenous aneurism observed by the writer in the Serbian army in 4 years, all operated on by him, 24 were of the direct type, artery and vein being in immediate communication. The common carotid artery was involved in 3 instances; the subclavian in 1; the brachial, 2; external iliac, 3; femoral, 13; and popliteal, 2. Often no hematoma around the affected vessels was found. Symptoms generally began only a few days and sometimes 1 or 2 weeks after the injury, the most characteristic sign being an audible thrill originating at the point

of communication of the vessels and transmitted centrifugally along the artery and centripetally along the vein. At operation, especially in cases of external iliac or femoral involvement, a pronounced dilatation of the vein at and above the point of communication was noticed; likewise, a narrowing of the arterial trunk below this point. Thus, a part of the blood brought by the artery, entering the vein, is transmitted by the latter, not in a peripheral, but in a central direction, toward the heart. The centripetal transmission of the thrill along the vein and the absence of peripheral varicosities are thus accounted for in these cases of direct arteriovenous aneurism. Soubbotitch (Bull. de l'Acad. de méd., May 30, 1916).

Treatment.—The treatment of arteriovenous aneurism is usually operative, as the disease is usually persistent and progressive. The artery may be clamped above and below the opening and the opening in the artery and vein closed by arterial suture. Where a thoracic aneurism is present the sac may be split and the communicating opening sutured from within the sac, as in Matas's aneurismorrhaphy. In some cases it may be necessary to ligate the artery above and below the point of communication. As a rule, the vein should not be ligatured.

In small traumatic aneurisms in which the distended inner coat of the vessel bulged through the external coats we have found it possible to reduce the hernia-like protrusion and to reunite the median adventitia by fine silk sutures, which reinforce the union by suturing adjacent connective tissue to the arterial wall.

Analysis of 161 cases of arteriovenous aneurisms published since 1889. The femoral was involved in 80 and the popliteal in 35 cases. Much better results are obtainable, as

a rule, from operating directly on the sac than from ligatures. The main drawback to a complete cure is the frequent coexistence of nervous lesions complicating the aneurism, which are generally solely responsible for the postoperative disturbances. Only when direct action on the sac is impossible should ligatures be given the preference. Removal of the sac offers the same advantages over incision for the arteriovenous as for the arterial aneurisms. Monod and Vanverts (Revue de chir., Oct., 1910).

In none of 15 cases of traumatic aneurism seen by the writer was he satisfied with simple ligature of the vessels, and the accompanying danger of relapse. The injuries in all were too complex and extensive to make it possible to carry out lateral suture in order to preserve the permeability of the arterial trunks. An essential condition for the performance of **extirpation** of arteriovenous aneurisms is to have a wide opening on to the aneurism; thus, for aneurisms in the axilla the pectoralis major was divided vertically; for aneurisms in the carotid region the sterno-mastoid was divided horizontally. These large divisions of muscle do not give rise to any serious functional trouble later if the divided ends are accurately sutured together at the end of the operation. Auvray (Bull. et mém. de la Soc. de Chir. de Paris, Apr. 20, 1915).

In 102 operations for aneurism due to war injuries the best treatment was found by the writer to be **suture** of the artery; it was performed in 74 cases; in most of the cases the suture was along the axis of the vessel; in only 3 cases was transverse suture performed. In arterial aneurism lateral suture was a simple operation. This was not the operation for arteriovenous aneurism. In 36 cases the wounded piece of artery was resected and the ends sutured circularly. Transplantation of a piece of vein to fill in the gap was not found necessary. Circular suture was easily per-

formed, even on the larger arteries; intima was applied to intima and a continuous suture inserted. Small arteries were ligated. Where large veins ran through infected aneurisms, they were ligated in 2 places and resected. Death occurred in 8 of his operated cases, 4 of the fatal cases being aneurisms of the subclavian. Bier (Beitr. z. klin. Chir., xcvi, 556, 1915).

In 13 cases of gunshot aneurisms treated by suturing the injured vessels, recovery was prompt and complete in all, and there have been no complications since. This result was also obtained in 25 of 29 cases in which the vessel was ligated, in 2 amputation was required later, and 2 others died from hemorrhage from an erosion. The circulation proceeds in all the cured cases with nothing to suggest that the men are not quite normal. von Haberer (Wiener klin. Woch., May 6, 1915).

In traumatic aneurism the best operation is considered by the writer to be quadruple ligation. It may be applied even in cases where there is perforation of the carotid at the bifurcation, when quintuple ligatures are applied; none of the cases so operated upon has been lost. Quénu (Bull. et mém. Soc. de chir. de Paris, xli, 592, 1915).

To *lessen the dangers of gangrene* after operation for aneurism, the writer resorts to the following method: The limb is made anemic by inhibiting the entire circulation below the aneurism for 2 minutes by means of a constrictor, then releasing the constriction and compressing the artery above the aneurism. If an active hyperemic reaction is obtained the collateral circulation is sufficient. L. Moszkowicz (Beit. z. klin. Chir., xcvii, 569, 1915).

Conditions related to aneurisms include certain nevi, cavernous angioma, aneurism by anastomosis, and arterial angioma or cirsoid aneurism. These conditions suggest new growths or tumors more than aneurisms. Some are congenital; others are acquired, and the aneurism by anastomosis, a vascular tumor consisting of involved arteries, veins, and capillaries, which may reach an enormous size, is present. The arterial angioma or cirsoid aneurism usually occurs upon the head about the time of adolescence. It may be congenital or follow traumatism. The arteries are enormously dilated and very tortuous; the bruit may be so loud as to interfere with the patient's sleep. These conditions are usually treated by **electrolysis, ligation,** or **excision.**

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ANGINA LUDOVICI. See PHARYNX AND TONSILS, DISEASES OF.

ANGINA PECTORIS.— DEFINITION.

—Angina pectoris (stenocardia, breast-pang) is the name given to a group of symptoms which usually depends upon organic disease of the heart or aorta. An attack consists in the sudden onset of agonizing pain in the precordial or sternal regions, accompanied by a feeling of constriction and in severe cases by a sense of impending death. The pain radiates into the back, the shoulders, and the arms, particularly the left. The patient is pale, haggard, motionless, and often bathed with cold perspiration.

SYMPTOMS.—Suddenly, after exertion, excitement, or a hearty meal, the patient feels an excruciating, burning, or tearing pain in the heart or beneath the sternum, accompanied with a sense of constriction (*angere,* to throttle), as if the heart were in a vise. The pain radiates into the back, upward into the shoulders, and

down the left arm, often even to the fingertips. It may be felt in both arms, in the neck and head, and even in the trunk and lower extremities. "In true angina the seat of the pain may be entirely away from the chest, and may be, as in Lord Clarendon's father, at the inner aspect of the arm, or about the wrist, or in rare instances confined to the side of the neck, or even to one testis" (Osler). After an attack, there may be tenderness above and outside the left nipple and in the left arm.

The pain is explained by James Mackenzie as a sensory reflex due to irritation of the 1st, 2d, and 3d dorsal and 8th cervical nerves, and the sense of constriction to reflex stimulation of the intercostal nerves.

Paroxysms occur in which pain is slight or absent (angina *sine dolore*). Early attacks are often of this sort. Later on there may still be no pain, or the paroxysms may sometimes be painful and at other times not.

A feeling of numbness accompanies the pain. There is a sense of impending dissolution. The sufferer sits or stands immobile and hardly dares to breathe. Yet there is no real dyspnea. The face is pale or livid; the forehead wet with perspiration. The pulse may remain strong and regular. Usually it is accelerated and of increased tension. A pulse of habitual high tension may be somewhat lowered during the attack (Mackenzie). The pulse may intermit or vary. Exceptionally it is slowed. The paroxysm lasts a few seconds or minutes,—sometimes half an hour or even several hours. At the end of it the patient often belches gas or vomits or has a movement of the bowels, with great relief. The in-

ference that indigestion has caused the paroxysm is natural, but probably erroneous; although it is true that even slight exertion directly after a meal may precipitate an attack.

The less found wrong with the heart upon examination, the more certain may one be of the diagnosis. In a series of 500 cardiovascular and cardiorenal cases there were 35 cases of genuine angina pectoris. One-third had succumbed to an acute anginal attack, and two-thirds to gradual cardiac death. J. E. Talley (Med. Rec., Nov. 6, 1915).

The cases may be divided into two groups: the angina of effort and the angina of decubitus, but in the later stages of either form of the disease the distinction becomes less clearly marked, and either form may rapidly be followed by the other. In determining what organic lesions may be present, very great importance is attached to the results of radioscopic examination. As a rule, in the angina of effort, aortitis is present. The qualitative changes shown by radioscopy are diminution of transparency of the walls of the aorta, which on the screen look either uniformly dark or sown with scattered dark patches. Very often there is more or less complete immobility of the vascular contours, indicating loss of elasticity in the vessel walls. Radioscopy may also reveal modifications in volume whose detection has escaped ordinary methods of observation. One change of much significance in the diagnosis of the epigastralgic form of the disease is enlargement of the aortic arch. H. Vaquez (Arch. des mal. du coeur, Mar.-Apr., 1915).

The attack may prove immediately fatal. If not, the patient is left exhausted, but regains his usual condition in a few hours or days.

The attack is almost sure to be repeated. This may happen in an hour or not for weeks or months. The length of the interval depends greatly

upon the persistence of the patient in avoiding the exciting causes. After a severe attack, rest in bed is desirable for several days, or, if the patient is much enfeebled, for a week or two. Successive paroxysms occur with gradually increasing readiness.

The diagnosis of angina pectoris, at least in its milder form, cannot be made from the history alone. The other forms of cardiac pain, of toxic or neurotic origin, the latter especially in women, may exactly simulate a true angina pectoris.

In diagnosing between true and false, organic or functional, there is one physical sign which the writer believes positive. It is so slight, and apparently so insignificant, that one almost hesitates to mention it. It is simply a slight clicking sound, of a harsh or rough quality, accompanying, or following at barely perceptible interval, the sound of aortic closure. It is not an accentuation of the closure sound of the valve, such as the loud, clean, "cork and bottle" aortic second sound, which is significant of high arterial tension. G. R. Butler (Archives of Diagnosis, Oct., 1909).

The most frequent exciting cause of seizures is overexertion, though walking, eating heartily, and emotional outbursts have also their etiological place. A sense of constriction without pain occurring after the ordinarily exciting causes is always highly suggestive. A striking fact is the frequency with which patients remain unwarned by experience of the dangers of carelessness. A large proportion of patients with embolic or thrombotic obstruction of a large branch of a coronary artery have died suddenly soon after the accident, and yet at autopsy pathologists have found evidence of long-standing obstruction. Coronary obstruction may cause an anginal seizure, and yet the patient not die at once nor even soon. J. B. Herrick and F. R. Nuzum (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 16, 1917).

While the physical pain of angina pectoris is the essential and initial manifestation of the syndrome, the angor, an expression of the high degree of emotional anxiety, is a close second. In certain particularly emotional subjects, the fright awakened by a slight attack of pain is so marked that the primary, essential manifestation may be overlooked by the examining physician. The fear of death in angina pectoris seems to result from the combined influence of the physical pain and the intense subjective exhaustion, which leads to the mental conception that, as some patients have expressed it, all the processes and activities of nature have ceased. R. Benon (Presse méd., Jan. 21, 1920).

DIAGNOSIS.—In true angina pectoris skilled observers almost invariably find evidence of organic cardiac or aortic lesion. In a supposed case these should be sought most carefully. Particularly to be looked for are arteriosclerosis, hypertrophy or dilatation of the left ventricle, aortic regurgitation, and feebleness of the muscular power of the heart with facial pallor, sometimes lividity, sweats, and coldness of the surface.

According to Mackenzie, angina pectoris is an evidence of an exhaustion of the function of contractility, the pain and reflex muscular contraction being reflex phenomena due solely to an impairment of the contractile function of the heart. This does not, however, explain the entire situation, for W. J. Pulley (N. Y. Med. Jour., Nov. 8, 1913) believes there must of necessity be present with it a great distress of the function of tonicity, if not a beginning impairment. The pains are protective, by causing the patient to cease muscular efforts, and tend to rest the heart. The fear also is protective by causing the patient temporarily to cease worries and excesses of all kinds. The flushed face, due to reflex stimulation of the vasodilators of the superficial capillaries, also tends to reduce vascular super-

tension. The contraction of the intercostal muscles is also protective; it prevents deep breathing, which increases the arterial tension, and provides a splint to protect the already stretched and weakened aortic walls. EDITORS.

Intercostal neuralgia causes pain along an intercostal nerve, not radiating as in angina pectoris. It presents points tender to pressure near the vertebræ and sternum and in the axilla. It is not associated with disordered circulation. It is more common in women than in men.

Gastralgia is apt to occur when the stomach is empty. The pain does not stream into the shoulder and arm. While there may be collapse and a sense of impending death, there is no evidence of heart disease. Like intercostal neuralgia it is likely to occur in anemic young women, rather than in middle-aged men.

On the other hand, the pain of true angina pectoris may be felt lower down than the precordia. And, as already stated, the termination of an attack may be marked by the discharge of gas. Particularly if there is no extreme cardiac pain, this may lead the patient, and in some instances has led his physician astray.

Cardiac asthma is dyspnea due to a weak heart and occurring more or less paroxysmally. Pain is not prominent. The picture is apt to include pulmonary edema, enlarged liver, and dropsy, and it could hardly be mistaken for angina pectoris. Mitral disease is not apt to be associated with angina pectoris, and relief from attacks is often experienced when a mitral leak develops in an aortic case.

The recognition of cardiac lesions observed after attacks of angina pectoris is of great importance, inasmuch as it leads the physician in charge to insist on perfect rest for the patient for days or even weeks after a severe attack, and thus prevents, in some instances, sudden death. The cases in which the attacks are followed by the appearance of clinical signs in the heart may be divided into three classes. In the first group there is a rise of temperature and a slight enlargement of the cardiac area of dullness. The fever may be slight, but if other causes are excluded it is of great value in the diagnosis of myocarditis following angina pectoris. In the second group there is, in addition to fever, a distinct dilatation of one or other of the cardiac cavities, which can readily be discerned on physical examination. Finally, in the third group, there develops an acute endocarditis following an attack. In spite of the fact that clinically the occurrence of acute endocarditis after angina pectoris is not a well-recognized phenomenon as yet, it has long since been described pathologically. Kernig (Roussky Vratch, Oct. 30, 1904).

"Pseudoangina."—Pseudoangina pectoris, or hysterical angina, occurs in females or neurasthenic men, usually under the age of 40, without evidence of organic cardiovascular changes. There are low tension, feeble second sound, and soft arteries. The attacks are spontaneous and are apt to be nocturnal and periodic (menstrual). They last an hour or two, being more prolonged than the true paroxysms. The patient is agitated, writhes, or walks about the room, and talks. The heart feels not constricted, but distended. The pain is not apt to be so severe as in true angina pectoris. Paresthesiæ and vasomotor symptoms are prominent. The patient's symptoms are sometimes colored by his having consulted encyclopedias and the like (Broadbent). Death never occurs.

Angina pectoris in its typical form is a rare disease. Pseudoangina, or cardiac asthenia, as it is frequently called, is much more common. It is erroneous to speak of angina pectoris as a neurosis of the heart, as in the great majority of instances there are organic changes in the coronary circulation, the cardiac muscle, or lesions of the aortic orifice. Neurotic angina is exceptional, is almost always associated with spasm, or with a sudden increase in intracardiac pressure. Beverly Robinson (Amer. Jour. Med. Sci., Feb., 1902).

Painless angina is much more common than one would suppose it to be from the infrequency with which it is mentioned; but, in all probability, the disease is not always recognized, and the patient's sufferings are attributed to hysteria or some reflex disturbance. When the symptoms are accompanied by a dilated right heart or distinctly atheromatous changes the diagnosis is easy, but when physical signs are absent it is difficult to arrive at an absolute opinion. If, when free from the paroxysms, the patient continually suffers from a feeling of weight or distress over the precordia, and has a tendency to take occasional deep inspirations, there is a strong probability that the right ventricle is affected, and this amounts to certainty if the symptoms are invariably produced or aggravated by exertion. This form of angina is entirely different from the painful variety, and in many instances demands a diametrically opposite treatment. W. W. Kerr (Jour. Amer. Med. Assoc., May 29, 1909).

Hysteria.—It should, of course, be remembered that hysteria may be combined with organic disease, and that a careful physical examination should be made in any suspected case; but the discovery of mitral disease would not be inconsistent with a diagnosis of pseudoangina.

There is a nervous form of syphilitic angina which is distinct from hysterical angina pectoris. The two conditions may be distinguished as follows: In hysterical angina the attacks come on, as a rule, at night; on examination there are found hysterical areas on the skin of the chest, and the attacks begin with paresthesia of such an area, and end in tears, sobs, and other manifestations of excitement. The syphilitic attack of the nervous type is preceded by fatigue, not by excitement. It is very important to distingish the nervous syphilitic type from the organic syphilitic angina, which depends upon a lesion of the heart muscle itself. The chief characteristic of these is the presence of periodic attacks of angina with dyspnea between the attacks. M. J. Breitman (Vratch, Nov. 14, 1900).

Hysterical angina pectoris is common, especially before the age of 40. It is most frequent in women. The crises in childhood are less severe than those of adult life. Almost anything may be the cause of the attack, even acute articular rheumatism. Frequent paroxysms are often noted about the menopause. Sometimes an attack occurs by suggestion from seeing a paroxysm in another. There is precordial pain, often with a distinct aura. The paroxysms occur at night, periodically. About the precordia is generally found an area of marked hyperesthesia. Palpitation, rapid pulse, and vasomotor symptoms are common. In fact the symptomatology is polymorphous. In some cases true aortitis or endocarditis may exist, yet the attacks of angina pectoris are hysterical. Mercklen (Médecine moderne, Apr. 23, 1902).

Syphilis.—A history of syphilis in a man, even if under 40 years of age, renders the occurrence of true angina pectoris less improbable than it otherwise would be, for there is a possibility of syphilitic aortitis obstructing the orifices of the coronaries.

Tobacco, Tea, etc.—Excess in tobacco (less often alcohol, tea, and coffee) and lead poisoning may occasion spurious angina, or again they may aggravate a genuine paroxysm depending on organic lesions.

While certain cases are evidently true angina and others equally obviously pseudoangina, some are extremely puzzling. All these attacks (true and "false") have this much in common, that for the time being the heart is unable to perform the work demanded of it; so that they differ more in etiology and prognosis than in immediate condition.

ETIOLOGY.—Males over 40 years of age in comfortable worldly circumstances make up the majority of sufferers from angina pectoris. Predisposing causes are: alcohol, syphilis (arteriosclerosis, tabes dorsalis), rheumatism, gout, diabetes, chronic nephritis, and bacterial infection (influenza, plague, malaria). Sometimes attacks are hereditary.

As exciting causes may be named: physical exertion, mental strain, profound emotion, and digestive disturbances.

The writer observed several cases of angina pectoris, in which hyperacidity of the gastric secretion was shown by an Ewald and Boas test breakfast with a bland meal taken the previous evening, and usually a glass of milk before retiring. These cases may explain the anachronism of an epigastric or abdominal angina pectoris, both an impossibility. He recalls Latham's view that angina pectoris is a cramp of the heart, excited by the hyperacid gastric juice through the filaments of the vagus; a fact which should not appear strange to any one familiar with the violent spasms excited by hyperacid secretion in spasmodic closure of the pylorus. This cardiac spasm may supervene in any and all the various forms of cardiac disease, which explains the many contradictions set forth by Allbutt. H. Illoway (N. Y. Med. Jour., May 25, 1918).

The attacks may appear in the daytime, especially at first; but some of the worst occur at night; so that finally the patient may dread going to sleep.

A point that stands out prominently in the writer's experience is the frequency of angina pectoris in physicians. Thirty-three of his patients were physicians, a larger number than all the other professions put together. Only 7 were above 60 years of age, one a man of 80, with aortic valve disease. The only comparatively young man in the list, 35, was seen nearly twenty years ago in an attack of the greatest severity. Worry and tobacco seem to have been the cause. He has had no attack now for years. Two cases were in the fourth decade, 13 in the fifth, and 11 in the sixth. Neither alcohol nor syphilis was a factor in any case; of the 26 patients under 60, 18 had pronounced arteriosclerosis and 5 had valvular disease. In a group of 20 men, every one of whom Osler knew personally, the outstanding feature was the incessant treadmill of practice, and yet every one of these men had an added factor, worry.

So far as symptoms are concerned, the writer's cases fall into three groups: 1, *les formes frustes;* 2, mild, and, 3, severe.

1. The mildest form, *"les formes frustes"* of the French, with substernal tension, uneasiness, distress, rising gradually to positive pain, is a not infrequent complaint, one, indeed, from which few escape, is associated with three conditions. Emotion is the most common and the least serious cause.

2. Under the mild form, angina minor, come 43 cases. Osler has grouped under these the neurotic, vasomotor, and toxic forms, the varieties which we formerly spoke of as false, or pseudo-, angina. The special features of this variety are: the greater frequency in women, the milder character of the attacks, and the hopeful outlook.

3. Severe angina, angina major, is represented by 225 cases, of which

211 were in men. Two special features here are, existence in a large proportion of all cases of organic change in the arteries and liability to sudden death. Osler (Jour. Amer. Med. Assoc., from Lancet, Mar. 12, 1910).

Angina from tobacco can be agonizing, but it always ceases with the withdrawal of the narcotic; where the angina persists despite this withdrawal, it is necessary to make a Wassermann test for syphilis. Three cases reported in which a positive reaction indicated the proper mercurial treatment, which was followed by immediate relief after other measures had proved inert. C. Feissinger (Semaine méd., Apr. 2, 1913).

The angina pectoris following overexertion is merely a primary dilatation of the left heart when the heart has been "forced." Tobacco can only evoke an attack with hitherto latent organic trouble, but is not capable of inducing the latter. Huchard found a history of syphilis in 35 of 150 cases of angina pectoris and the author in 30 of 100, and this before the Wassermann reaction was known. H. Vaquez (Arch. des Mal du Coeur, Mar.-Apr., 1915).

An analysis of 178 cases showed that the great majority of them occurred between the ages of 55 and 64. In 26 per cent. no definite lesion was detected either in the heart or in the aorta. In 24 per cent. there was a valvular lesion, and in 25 per cent. there were aortic dilatation and aneurism. Bramwell (Edinburgh Med. Jour., Dec., 1915).

PATHOLOGY.—It is exceptional

for attacks of true angina pectoris to be observed in persons presenting no evidence of organic circulatory lesion. The commonest underlying conditions are sclerosis of the coronary arteries, degeneration of the myocardium, cardiac hypertrophy, atheroma of the aorta, aneurism of that vessel near its origin, and aortic regurgitation. There is, however, "hardly an affection of the walls or cavities of the heart, scarcely a morbid condition of the arteries that nourish it or spring from it, with which the distressing malady has not been observed to be associated" (Da Costa).

Recent writers lay stress on obliteration of the lumen of the coronary arteries as the essential basis of true angina pectoris, which obliteration may be occasioned either by sclerosis of the vessels or by changes in the aorta at their origin. "So intimately associated is the true paroxysm with sclerotic conditions of the coronary arteries that it is extremely rare apart from them" (Osler). Huchard held the same view.

The pain of angina depends upon vascular distention in the mediastinum, which is the result of a more or less localized vasodilatation and of a more or less generalized peripheral vasoconstriction. It would seem that the angina is not due to the organic lesions any more than is asthma due to emphysema, or migraine to atheroma of cranial vessels. The connection between the organic lesions and angina should then be ascribed to the chronic peripheral vasoconstriction, which constitutes the earliest stages of many forms of chronic organic disease of the heart and vessels.

Preventive treatment resolves itself into the prevention of exaggerated peripheral vasoconstriction, continuous or recurrent. Purin-free diet, cutting down of the intake of carbohydrates, especially the saccharine carbohydrates, and the fats, is advocated. Francis Hare (Med. Rec., Oct. 20, 1906).

Angina results from an alteration in the working of the muscle-fibers in any part of the cardiovascular system, whereby painful afferent stimuli are excited. Cold, emotion, toxic agents interfering with the orderly action of the peripheral mechanism, increase the tension in the pump walls or in the larger central mains, causing strain, and a type of abnor-

mal contraction enough to excite in the involuntary muscles painful afferent stimuli. Mackenzie suggests that there is rapid exhaustion of the function of contractibility, which is, after all, only the fatigue on which Allan Burns laid stress. In a disturbance of this Gaskellian function is to be sought the origin of the pain, whether in heart or arteries. In stretching, in disturbance of the wall tension at any point, and in a pain-producing resistance to this by the muscle elements lie the essence of the phenomena. In a man with arteriosclerosis and high pressure, and all the more likely if he has a local lesion, a syphilitic aortitis for example, disturbance, at any point, of the tension of the wall permits the stretching of its tissues. Spasm or narrowing of a coronary artery, or even of one branch, may so modify the action of a section of the heart that it works with disturbed tension, and there are stretching and strain sufficient to arouse painful sensations. Or the heart may be in the same state as the leg muscles of a man with intermittent claudication, working smoothly when quiet, but instantly an effort is made, or a wave of emotion touches the peripheral vessels, anything which heightens the pressure and disturbs the normal contraction brings on a crisis of pain. Osler (Lancet, Mar. 26, 1910).

The writers observed a man of 34, who developed attacks of angina pectoris and died in 5 months. There was no trace of venereal disease or alcoholism, but signs of tobacco poisoning had been so pronounced that his daily ration of cigars and cigarettes was reduced. The case would have been cited as one of fatal tobacco poisoning but necropsy revealed syphilitic lesions in the aorta partly closing up the openings into the coronary arteries. Mouriquand and Bouchut (Arch. des Mal. du Coeur, Oct., 1912).

The writer does not deny all significance to the prevailing doctrine of coronary sclerosis, but its meaning has hitherto been virtually negative.

The hypothesis of Mackenzie is untenable. Angina pectoris does not mean a want of muscular strength, of contractility, but the result of "brusque hypertension in the left ventricle, both systolic and diastolic from the increased tone, together with an unregulated and disordered excitability" of the "primitive fascia and of the cardiac nerves." Castelli (Riv. crit. di clin. med., Dec. 6, 1913).

Heberden—who introduced the name of angina pectoris for the affection—declared in 1768 that its most common termination is sudden death. This holds good today, yet we are unable to state the rationale. In 1889 McWilliam advanced the belief that in many cases of sudden death a myocardial fibrillation could be invoked as the efficient cause; but only recently have animal experiments given some corroboration to this view. Sudden death in angina pectoris is considered by the writer to be the result of ventricular fibrillation, but the direct actual proof can be supplied only by electrocardiography. The patient does not die from paralysis of the heart but from the direct opposite, the excessive production of impulses. We already have data which shows that angina pectoris occurs only when there is temporary ischemia of the heart, and we know by experiments on animals that this ischemia is liable to precipitate fibrillation of the ventricles, and also that the ischemia predisposes the heart to fibrillation. Hering (Münch. med. Woch., Nov. 2, 1915).

The immediate, precipitating conditions of a paroxysm are not known, but they are supposed to be connected with disturbances of the vagus, or, perhaps, the sympathetic nerves. Nothnagel reported a series of cases under the title "angina pectoris vasomotoria" which seemed to be due to a pure neurosis. They followed exposure to cold, and were ushered in by spasm of the peripheral arterioles, which presumably

produced the cardiac disturbance because of the increased exertion demanded of the heart in order to propel the blood through narrowed channels.

Broadbent describes angina vasomotoria as a comparatively favorable class of cases of high arterial tension associated with general arteriosclerosis and a hypertrophied heart capable of powerful contraction. "The circulation in the coronary arteries may be sufficient for ordinary needs, but when the arterial tension is further raised by exertion or increase of peripheral resistance attacks of angina are induced."

From a neuralgia or a neurosis true angina pectoris differs in being frequently fatal, in attacking men ten times as often as women, and in being associated with organic changes in the neighboring structures, viz.: the heart and aorta.

Lesions of the cardiac plexus and the branches of the vagus have been found in repeated instances of angina pectoris, but that such lesions are invariably present and essential to the disorder has not yet been proved. "The cardiac nerves may be seriously implicated in aneurism, in mediastinal tumors, in adherent pericardium, and in the exudate of acute pericarditis, without causing the slightest pain" (Osler).

The late Sir Benjamin W. Richardson regarded angina pectoris as an actual disease analogous (as Trousseau held) to epilepsy, and due to a disturbance in the sympathetic nervous system.

Attention called to the coincidence of disturbances in circulation elsewhere. In a man of 33, angina pectoris, Raynaud's disease, loss of 1 eye from disturbance in the circulation in the retina, and intermittent claudication occurred in turn. The first symptoms were an attack of angina pectoris after a bombardment. These conditions were all on the left side, a fact which points to a nervous origin for them all, and seems to exclude local endarteritis. The attack in the fingers was brought on by cold, the attack in the toe by walking, the angina pectoris by fatigue and emotions. The fatal outcome in this case shows that even attacks with a nervous origin may prove fatal and that spasm of the artery capable of producing total anemia in a finger can well arrest the heart. Bard (Presse méd., Jan. 26, 1921).

Debove says that in tabetic angina pectoris there is no organic lesion of the heart or large vessels, and that the attack must be regarded as a visceral crisis. Dana refers cardiac crises in tabes to a degenerative irritation of the vagus. It should, however, be remembered that aortic disease is rather frequent in tabetic patients.

In regard to the causation of attacks of angina pectoris in the graver cases which are associated with serious structural disease of the heart and vessels, J. Burney Yeo states that in by far the greater number of deaths from organic disease of the heart all the various lesions may be present which have been found in fatal cases of angina and yet no true anginal attacks have ever been complained of. In his opinion there is some additional circumstance needed to account for the angina. The most serious forms of angina seem to have a complex causation. First, there must be a neurosal element; the nerves of the cardiac plexus suffer irritation, and an intense cardiac nerve-pain is excited; this acts as a shock to the motor nerves of the heart, and thus reacts on the heart-muscle, which, in fatal cases, is already on the verge of failure from organic causes; and, if there should be excited at the same time some reflex arterial spasm, the heart will have to

encounter an increased peripheral resistance as well. In such cases the rapidity of the fatal issue is no argument against the neuralgic nature of the angina. In certain conditions, especially in habitual high arterial tension, strain is apt to fall (when the aortic valves are competent) rather on the first part of the aorta than on the ventricular surface, and anginal attacks are more prone to occur in these cases, as this part of the aorta is in such close relation with the nerves of the cardiac plexus, rather than in those cases in which the strain is felt on the interior of the cardiac cavities.

The causation of the less grave and more remediable forms of angina is also, in many instances, complex. A cardiovascular system feeble and poorly nourished on account of anemia may be submitted to undue strain; or there may be some intoxication—such as that of tea, tobacco, alcohol, gout, or some intestinal toxin—irritating the cardiac and vasomotor nerves, increasing peripheral resistance, and so exciting anginal attacks, which may altogether pass away and be completely recovered from. Vasomotor spasm as a unique cause of attacks of angina must be set aside as inconsistent with extended clinical experience.

Cases of angina pectoris, both of the milder and graver forms, occur without any evidence of vasomotor spasm or of heightened arterial tension; and the conditions of heightened arterial tension, together with a feeble cardiac muscle, very commonly coexist, without any tendency whatever to the development of anginal attacks. The argument in favor of a vasomotor causation has been inferred from therapeutic experiment and the relief to the paroxysm which has attended the use of agents which cause arterial relaxation. But most, if not all, of these vasodilators are also anesthetics, and, as Balfour has pointed out, it is probably to their anodyne action on the sensory cardiac nerves that they owe their chief efficacy; Grainger Stewart also has pointed out that nitrite of amyl has a direct effect on nervous structures, and that it relieves other forms of neuralgia.

Certain fallacious conceptions of angina pectoris prevail. Thus, in true cardiovascular angina pectoris, peripheral arterial sclerosis, cardiac hypertrophy, and high blood-pressure are essential. This is by no means always the fact. Arterial change may be widespread and the coronaries sclerotic without hypertrophy of the heart or rise in blood-pressure. The sclerotic or atheromatous process may be quite limited, localized to the beginning of the aorta, and only encroaching a little on the coronaries, while the peripheral vessels may be normal. Especially in syphilitic cases are the conditions liable to be thus localized. In some of the most serious cases there may be no abnormal arterial pressure, indicating, perhaps, a weakened cardiac muscle. The finding of aneurism or lesion of the aortic valves does not exclude angina, but is rather in its favor. The attacks are not always few in number, and following exertion, and life is not necessarily cut off within a few months after the appearance of the disease. Patients may live a number of years with comparatively frequent attacks. While comparatively rare in women, the disease is by no means unknown, and serious mistakes may be made in diagnosis, especially in nervous and hysterical cases. The cardiopath is often a neuropath also. Pain is not always excessive. It may be mild or even lacking; its radiation is variable. Even in fatal cases there may be no constant pain. Unconsciousness, though unusual, is seen at times, and, while the patient usually is afraid to move, and will not lie down, there are exceptions to this rule. Eructations or vomiting during an attack do

not prove it to be a false angina and not organic or cardiovascular. While the disease is very grave, there is no certainty that death is imminent. The kidneys, as well as the heart, must be investigated as regards prognosis. J. B. Herrick (Jour. Amer. Med. Assoc., Oct. 22, 1910).

PROGNOSIS.—The underlying condition is apt to prove fatal eventually, and it may end life in the first paroxysm; but a careful regimen may prolong existence for years, and Flint, Bendel, and Labolbary have each reported cases of recovery.

The signs of danger during any particular attack are the subjective sense of impending death and the feebleness and irregularity of the pulse. The general prognosis is, of course, influenced by the stage which the organic circulatory changes have already reached.

The pseudoattacks are apt to be repeated oftener than are the genuine, but the prognosis is good, both as to life and as to the final disappearance of the trouble.

In common with all other observers, the writer finds that angina pectoris is more common in the male than in the female, in the ratio of 63 to 48. The youngest patient in his series of cases was 29 years old; the oldest, 76. The longest duration of the recurring syndrome was seventeen years; the shortest was found in three who died in the first attack.

In the cases of angina in which coronary sclerosis alone existed we find 3 dead in the first attack and 7 others dead. Of the latter, 2 died of diabetic complications, 1 of complicating pneumonia in the status anginosus, death being due to acute cardiac dilatation, 1 of a cerebral and another of a gastric hemorrhage. So that, in all, in only 6 cases could death be attributed to the coronary sclerosis. The duration of the disease in these cases varied from sixteen months to seventeen years, and all were males. In the 29 cases of coronary sclerosis there is but 1 female.

When the obstruction is due to thrombosis or embolism, the attack is usually fatal, either immediately or later on, as the result of changes in the myocardium. The attack is always immediately fatal when one coronary artery is closed. As a rule, death occurs instantaneously where the descending or circumflex branches are completely closed, but occasionally the patient survives for a few days, as is shown by myocardial infarcts found *post mortem*. Forchheimer's experience leads him to believe that when both cardiac asthma and angina pectoris are present from the onset the outlook for improvement is very small. But he does not agree with Neubürger, who states that in coronary sclerosis there are 3 stages of myocardial changes, which develop and which are always fatal.

So far as the duration of the disease is concerned, aside from those who died in the first attack, in 8 the disease lasted from one to two years; in 4 from two to four years, and in 1 for seventeen years. Of those alive, 4 have had the disease from eight to ten years, the same number from five to eight years, and 10 from four to five years. F. Forchheimer (Jour. Amer. Med. Assoc., from Ill. Med. Jour., May, 1910).

TREATMENT.—During a paroxysm the first remedies to employ are such as will dilate the arterioles. **Nitrite of amyl** is the best because it acts with the greatest rapidity. A "pearl" of this drug may be crushed in a handkerchief or in cotton placed in the bottom of a glass tumbler, and inhaled. **Nitroglycerin** may be injected subcutaneously ($\frac{1}{100}$ to $\frac{1}{50}$ grain), or a tablet of this substance may be masticated, or a minim of **spiritus glycerylis nitratis** may be placed upon the tongue. It is readily absorbed from the mouth and acts

almost as quickly as when given hypodermically. **Erythrol tetranitrate** has an action like nitroglycerin, but milder and decidedly more prolonged. It may be given in tablets of ½ to 2 grains.

The **nitrites** are sometimes marvelously efficacious in checking an attack, and their failure to give benefit does not exclude true angina. In some cases **digitalis** does more good than all the nitrites or iodides, and in this the writer's experience agrees with that of Romberg, who advised it in some cases. J. B. Herrick (Jour. Amer. Med. Assoc., Oct. 22, 1910).

The writer has long been convinced that the absorption of toxic products during metabolism is an etiologic factor of importance in the pathogenesis of all functional troubles of the heart and of the aorta. In 123 anginal patients, 80 of whom have been followed for a sufficient time to warrant therapeutic conclusions, dietetic treatment intended to avoid toxemia was used. The first day, the patient having angina pectoris attacks is given nothing but **water.** On the second day **milk** is given in quantities varying from 1½ to 3 quarts. Nothing but milk is allowed for from 1 to 3 weeks, according to the severity of the case and the response to treatment. In the milder cases, at the end of a week, soups made of milk and various kinds of **cereals** are added and continued for 1 or 2 weeks. At the end of this time cooked vegetables without salt are added and continued for a month or two. Then eggs and a small amount of meat are allowed. Milk still remains the basis of the diet, and no salt is added to the food. Soca (Arch. d. mal. du Coeur, Aug., 1915).

The theory that the real seat of the disease is usually in the arterial walls and often in the external coat accounts for the incidence of the pain much better than the older view that the disease resulted from an affection of the coronary arteries with degeneration of the myocardium.

The prognosis is more hopeful than is generally believed, under proper care and treatment, *a very important part of which is abundant rest with heart tonics as needed.* In the treatment, nitrates are among the most valuable remedies, but they are usually given in insufficient doses. The sublingual administration of fresh hypodermic tablets of **nitroglycerin** is of great value in relieving pain. It is of the utmost importance that these tablets should be fresh and that they should be given in sufficiently large doses. Given sublingually, the full effect of these tablets is experienced in from 1 to 3 minutes, whereas taken into the stomach the efficiency is reduced by half and the effect delayed for about 10 minutes. When an attack comes on 2 or more tablets of $\frac{1}{100}$ grain (0.00065 Gm.) of nitroglycerin should be taken at once and repeated every few minutes until the desired effect is obtained. The effect of amyl nitrite is not as certain as nitroglycerin. Sodium nitrite seems to possess some toxic property and is liable to disturb the stomach. Erythrol tetranitrate was found to cause more headache and did not relieve the pain as promptly as nitroglycerin, although its effects may be of longer duration. The heart may be protected against inhibition shock by the use of **atropine** in doses as much as $\frac{3}{100}$ grain (0.002 Gm.) may be needed for some adults. E. Fletcher Ingals (Jour. Amer. Med. Assoc., Apr. 6, 1918).

Relief by these means is often immediate; but, if not, **ether** should be inhaled. **Chloroform** is also advised by excellent authorities. Flint thinks it not without danger, if the heart is weak; ether, on the other hand, is a stimulant. **Morphine,** subcutaneously, is a valuable and sometimes an indispensable remedy. Whittaker advises that it be given with caution in a condition which may anyway terminate in sudden death. The

morphine (¼ grain) may be guarded by atropine (¹⁄₅₀ grain), and in case of alarm also by strychnine (¹⁄₃₀ to ¹⁄₂₀ grain). Electricity has also been recommended.

Factors capable of bringing on the pain should be carefully avoided; every renewal of it keeps up the sum of stimuli. If for this end absolute stillness in bed be required, then bed it must be, with the corresponding reduction of food. If at first the attacks are not abolished, they will be mitigated, and will gradually taper off. All measures, medicinal, dietetic, etc., known to reduce arterial pressures should be enforced. Sir Lauder Brunton's potent means, the nitrites, are indispensable. To guard against vagus inhibition, atropine must be administered regularly. In very painful cases morphine may be needed also. An ice-bag applied cautiously and intermittently to the upper thoracic spine may prove helpful. The cause then requires treatment. Of new remedies two have seemed in the author's experience to be efficacious, more especially in angina minor— namely, (a) the high-frequency current, and (b) the administration of the lactic acid bacillus by the method of Metchnikoff. Baths and massage cannot be prescribed in any urgent stage of the disease. Causes of eccentric irritation must be discovered and neutralized. The patient must be warned never to swallow quickly, nor to bolt large morsels. Diuretin and aspirin have their advocates. Chloroform is very dangerous in angina. In syncopic failure of the heart artificial respiration should be tried. Allbutt (Brit. Med. Jour., Oct. 16, 1909).

Although the writer applied the Wassermann test in many cases of true angina pectoris, he obtained a positive response in only 33 per cent. Yet, after treatment as for syphilis there were no further attacks in 90 per cent. of the cases. In some there was a slight return of the pains later, but they subsided anew on resump-tion of treatment. Arsphenamin should not be used, as it brings on serious disturbances with aortic lesions. He obtained the best results with mercurial treatment in minute doses, on alternate days, in a series of 15 cases. Josué (Paris Méd., July 5, 1919).

Hot and stimulating applications over the precordia, such as a strong mustard poultice, are appropriate, as are also heat and friction for the extremities. Sometimes an ice-bag is put over the heart. By some it is preferred to heat. Alcohol and aromatic spirits of ammonia are of benefit in case the cardiac action is feeble. Syncope demands such drugs as digitalin, caffeine, strychnine, and camphor, employed hypodermically.

Good results obtained from theobromine in angina pectoris. In 1 case a man of 46 had been suffering for 2 months from repeated attacks of angina pectoris, recurring so constantly that he did not dare to go to bed; the attacks only lasted a few minutes, but had already induced great debility and distress. Examination revealed insufficiency of the aortic valve. He was given 0.5 Gm. (7.5 grains) of theobromine, and the dose was repeated at bedtime. There were no further attacks then or later. The treatment with theobromine must be long kept up, for months and years. Marchiafava (Policlinico, Feb. 28, 1909).

Prolonged rest in bed advocated in true organic cases. Marked improvement noted in most of the 20 cases studied. The patient should remain in bed at least 2 weeks, prolonged to 6 or 8 weeks in cases that cannot walk without bringing on anginal pain. Milk diet to be imposed from the start; later farinaceous foods added. Drug medication by theobromine, nitroglycerin, and even morphine and digitalin also utilized. Greatest improvement in old patients and those losing weight during treatment; least,

in cases with associated aortic insufficiency. Fiessinger (Bull. de l'Acad. de méd., Nov. 29, 1910).

The present writer has known **oxygen** to contribute to a favorable result in collapse due to chronic myocarditis with dilatation of the left ventricle, and it might be well for a subject of angina pectoris to keep some ready in his house.

> The painful attacks incident to cardiac disease, such as angina pectoris, also paroxysms of tachycardia, can be mitigated by causing the patient to belch up wind from the stomach, owing to the fact that the heart and the stomach are both innervated by the pneumogastric nerve. **Eructation** is produced by the following procedure: The patient, seated, takes a small drink of water and holds it in his mouth. He then throws his head as far backward as possible and swallows the water. The posture is such as to stretch the esophagus and induce in the pharynx a sensation which causes eructation, provided the result is not voluntarily prevented by the patient. It is well to warn the person that an eructation is desired; otherwise, he may restrain it out of a sense of decency. Max Herz (Semaine médicale, June 3, 1908).

> Dyspeptic disturbances are responsible for or at least aggravate angina pectoris in many cases. Great benefit can be derived from **magnesium oxide** and **peroxide** to neutralize abnormal production of gases and the gastric juice, and promote bowel functioning. Chlapowski (Med. Klinik, June 5, 1910).

Between attacks it is of vital importance to avoid the predisposing and exciting causes. **Rest** and moderation are demanded, especially after meals. As for drugs, **nitroglycerin**, taken after meals in doses just short of causing headache, has a distinct inhibitory effect upon the paroxysms. In some instances it might be better to order it every three hours, as its influence is not long continued. **Nitrite of sodium** (2 to 5 grains) may replace nitroglycerin.

Laxatives and **eliminative treatment** by **alkalies** are often of great value.

Surgical treatment of angina pectoris is advocated by Jonnesco.

> The phenomena of angina pectoris are caused by irritation of the cardio-aortic plexus due to a constant lesion of the aorta. By breaking the centripetal route between the cardio-aortic apparatus and the nerve centers by **resecting** the **cervical sympathetic nerve,** the advent of the aortic reflexes in the nerve centers and the reaction of these centers can be prevented. The writer performed a resection of the left cervical sympathetic in a case of angina pectoris. A definite cure resulted. Because of the brilliant result from the unilateral operation, he believes that a resection on the left side will usually be sufficient, but as the operation is simple and harmless, it is preferable to perform it on both sides. T. Jonnesco (Presse méd., xxix, 193, 1921).

The persistent use of **potassic iodide** is very effective. Ten or fifteen grains may be given thrice daily before meals in half a glassful of water; or twenty grains three times a day for twenty days, followed by **nitroglycerin** for ten days. The iodide is believed to dilate the arterioles and to promote arterial nutrition. Sée supposed that also by enlarging the caliber of the coronary arteries it invigorated the myocardium.

Arsenic and **phosphorus** in small doses also tend to avert the paroxysms. In case of fatty degeneration of the heart they would be contraindicated. **Barium chloride** in doses of $\frac{1}{10}$ to $\frac{1}{5}$ grain after meals is a good tonic for cardiac inefficiency, and often relieves cardiac pain.

Quinine and **methylene blue** have also been recommended.

The treatment by **saline baths** and by the **Schott method of exercises** has a most potent effect in improving the condition of the cardiac muscle and vessels, and appears to have a direct effect in making the attacks less numerous and severe, and even in causing them to cease during a period of months or years. The movements must be made with especial care and caution in these cases, and the resistance at the onset must be at a minimum. The artificial saline baths should contain from 1 to 3 per cent. of salt, and from $\frac{1}{4}$ to 1 per cent. of chloride of calcium, and should gradually be strengthened by the addition of **carbonic acid.**

Massage three times a week and persisted in for months may be of great benefit.

In most cases it is best to prohibit alcohol.

The cardiac tonics—**sparteine, strophanthus, strychnine, valerian,** and in suitable cases **digitalis**—are of the greatest utility.

The general tendency to anemia and defective oxygenation must never be lost sight of, and general **tonics,** including the use of **oxygen gas,** will be of excellent service.

Attacks of pseudoangina may be treated with **asafetida, ammoniated tincture** of **valerian, or compound spirit of ether,** and the outward employment of **heat, friction,** and **rubefacients.** Sometimes recourse must be had, however reluctantly, to **morphine.** The statement in clear and decided language of a favorable prognosis is of great benefit. Between attacks the underlying condition should be carefully sought and treated.

The frequent and indiscriminate use of such terms as false angina pectoris, angina sine dolore, angina vasomotor, etc., gives no clear sense of their etiology or pathology. The treatment should be based on these as follows:—

Hypertensive Cardiovascular Disease with Myocardial Insufficiency.—In this group the usual cardiac changes are ventricular hypertrophy, usually left, but sometimes right also; a patchy fibrous myocarditis; thickened aortal and mitral cusps; lime deposits on the first portion of the aorta and atheroma and thickening of both coronaries. There is a systolic blood-pressure of about 190 mm.; rough systolic first and sharply accentuated second sound at the right base; heaving apical impulse; urine with or without albumin or casts; varying grades of edema and visceral congestion; dyspnea usually upon excretion. The pains are commonly dull, most marked in the precordium and radiate to the neck and arms. As to the cause of the pain, it seems to be due to nutritional cardiac disturbance from inadequate coronary circulation. The author depends mainly on **digitalis,** preferably the tincture, given in 15-minim (1 c.c.) doses 3 times a day, continued even when pain and other symptoms disappear, for an indefinite period. Mental excitement and stress should be avoided. For the edema, **theobromin sodium salicylate** in 1-gram (15-grain) doses *t. i. d.,* on alternate days in water or in wafers are recommended. The **Carrel diet** was an excellent aid. In cases in which a luetic condition is proved or suspected the **iodides** are useful, otherwise they proved of no value in the relief of the pain.

Hypertension and Myocardial Insufficiency with Unstable Vasomotor Mechanism.—This is a smaller group with the highest systolic blood-pressure, around 180, and marked diurnal variations, precordial pains following exercise. Emphysema and myocarditis are the main pathological entities. Experimental subcutaneous

injections of **nitroglycerin** in doses of ⅟₅₀ grain (0.0013 Gm.) *t. i. d.*, has a marked temporary effect upon the blood-pressure and usually upon the symptoms. This or other vasodilators given at the onset of pain are likely to give great relief. Digitalis was not as beneficial as in Group 1.

Uremic Group.—This group is characterized by headache, nausea, vomiting, varying grades of anemia, paroxysmal, dyspnea, precordial distress, high systolic and diastolic pressure, nocturnal polyuria, and changes in the retina. The precordial pains are not relieved by nitroglycerin, digitalis, or diuretin. The pains are apparently caused by retained excrementitious products in the circulation. Dietetic measures, especially **low protein and high carbohydrates,** are of most value.

Acute Rheumatic Endocarditis and Rheumatic Endocarditic Exacerbations. —These cases usually occur in young persons with mild tachycardia, no dyspnea or decompensation, and with marked auscultatory evidence of valvular disease, usually mitral stenosis. There were "sticking" pains in the heart itself, and usually, no Head's zones. The rapid heart action and the precordial pain seem due to fresh exacerbations of endocarditis. The best medication is **sodium salicylate** in 1-Gm. (15-grain) doses hourly until 6 doses have been taken or tinnitus occurs. **Bromides** in moderate doses are helpful; absolute rest is necessary.

General Circulatory Failure and Decompensation from Endomyocardial Disease.—The cause of the precordial pain is apparently the nutritional disturbance in the heart, due to circulatory failure. Head's zones are often present. The treatment indicated for the first group is also indicated here.

Embolic Infarcts in the Main Coronaries and Their Branches.—In several cases with intermittent pains lasting days or weeks, the symptoms were possibly caused by embolic infarcts of the coronaries of the second or third order. There was a rise of temperature, acute endocarditis, progressive tendency of the disease, and tender local precordial areas.

Cardiac Lues.—This is a very frequent cause of precordial pain. The latter is usually substernal, dull, boring, and aching. It may, however, have the distribution of the types already described. Head's zones are rare. The main pathological changes occur in the aorta and myocardium. **Salvarsan combined with** the usual **mixed treatment** is of great value.

Premature Arteriosclerosis. — This rare group found in young adults, is characterized by persistent precordial distress, lasting often for months. Gastric symptoms similar to those of hyperacidity may predominate. Physical examination affords no hint of the severity of the pathological process. The cause for the sclerosis is still undetermined, but it may be the result of some infection and toxemia. Except **digitalis** for temporary relief, treatment is of no avail.

Tabacism.—The pains may be dull and aching, or sharp and radiating. The first premonition may be very sharp lancinating precordial pains radiating to the left shoulder and forearm and accompanied by unconsciousness. Most tobacco pains and arrhythmias cease when smoking is stopped. Occasionally they recur. **Nitroglycerin** given regularly or with the onset of pains is sometimes of benefit. S. Neuhof (Med. Rec., Jan. 15, 1916).

HERMAN F. VICKERY,
Boston.

ANGIOMATA. See BLOOD-VESSELS, TUMORS OF.

ANGIONEUROTIC EDEMA.
See ASCITES AND EDEMA.

ANHALONIUM LEWINII
(Mescal Button).—The mescal button is obtained from a plant growing in the valley of the Rio Grande, in Mexico. The

plant is of the family Cactaceæ. The tops of the plant when dried constitute the commercial **Anhalonium Lewinii**, first introduced by Lewin. The buttons or seeds are brownish in color, shaped like a top, and from 1 to 1½ inches in diameter. They are hard and can be pulverized in the mortar only with difficulty. In the mouth, however, under the action of the saliva, they swell and rapidly become soft, imparting a bitter, nauseous taste and causing a marked sensation of tingling in the fauces. Four alkaloids,—**mescaline, anhalonine, anhalonidine,** and **lophophorine,**—closely similar in their physiological effects, have been extracted from this species of anhalonium. From the related plant **Anhalonium Williamsi** the alkaloid **pellotine** is derived.

PREPARATIONS AND DOSE.—The following preparations may be used: Tincture (10 per cent.); dose, 1 to 2 drams (4.0 to 8.0 c.c.). Fluidextract (100 per cent.); dose, 7½ to 15 minims (0.5 to 1.0 c.c.). Powder; dose, 7½ to 15 grains (0.5 to 1.0 Gm.). The tincture and fluidextract should be made according to the processes prescribed in the United States Pharmacopœia for such preparations.

PHYSIOLOGICAL ACTION.—Lewin found anhalonium to be an intensely poisonous drug. A few drops of the decoction used by him in the frog sufficed to produce almost instantly changes consisting chiefly in the appearance of shrinking of the body, so that the batrachian seemed to pass into a mummified condition. Simultaneously, the animal raised itself upon its extremities and remained standing in this position like an ordinary quadruped, or crawled about. After fifteen minutes this spastic condition passed off and the frog rapidly returned to the normal state. When larger amounts were given death occurred in tetanic rigidity. The symptoms produced seemed closely allied to those of strychnine, Lewin noting that even after the spinal cord was severed peripheral irritation induced tetanus. In pigeons it was found that the drug produced convulsive vomiting in a few moments when injected hypodermically. The bird spread its wings, crouched down to the ground, and when disturbed exhibited muscular twitchings. Later the head was

drawn sharply back, the mouth opened widely, and general convulsions appeared. When death occurred the heart was always found in diastole. In rabbits the symptoms resembled those of strychnine poisoning.

In the human subject anhalonium in large doses produces an effect in some ways closely resembling that of Indian hemp: visions ranging from flashes of color to beautiful landscapes and figures, illusions of time and space, etc. This and related plants are employed as intoxicants by certain Mexican Indians in connection with religious ceremonies. According to Prentiss and Morgan, color effects constitute the main feature of the drug's action on the brain. Consciousness remains unimpaired throughout its effects. Mitchell states that sometimes symptoms resembling the visual phenomena of ophthalmic migraine are experienced. The aftereffects were also found by him to be markedly unpleasant, nausea and headache appearing which lasted for several hours. Heffter in 1898 carried out investigations on himself with the object of determining which of the active ingredients of mescal produced the visual hallucinations. An alcoholic extract of the buttons equivalent to 4½ drams was taken, and afterward a corresponding amount of each of the alkaloids. The symptoms produced both by the alcoholic extract and by mescaline (1½ grains) were colored visual hallucinations, slowing of the pulse, pupillary dilatations, loss of time relations, heaviness of the limbs, nausea, and headache. Anhalonine and anhalonidine in like amounts induced sleepiness without visual phenomena, while lophophorine (3/10 grain) caused occipital headache, facial redness and burning, and a temporary slowing of the pulse. Mescaline was thus shown to be the active constituent of anhalonium in respect of the visual phenomena.

According to Dixon, who carried out careful pharmacologic studies of anhalonium in frogs, cats, and rabbits and witnessed its effects in man, the chief effects of the drug in therapeutic doses appear to be: (1) Direct stimulation of the intracardiac ganglia; (2) initial slowing of the heart; (3) elevation of arterial tension; (4) direct stimulation of the brain centers

and of the motor spinal centers, as shown by an increase in reflex excitability.

Full doses of anhalonium induce motor weakness and inco-ordination. In still larger doses difficulty of respiration appears. Lethal doses, Dixon found, produce complete paralysis, and death is caused by respiratory failure.

THERAPEUTIC USES.—Prentiss and Morgan employed anhalonium in various conditions dependent upon **excessive nervous iritability,** with considerable success. While not a hypnotic in itself, the drug in therapeutic doses (7 to 15 grains) often removed the cause of the **insomnia,** and thus conduced to natural sleep. It has been credited with beneficial effects, especially in **neuralgic headache, acute delirium, mania, melancholia** and **hypochondriasis, hysteria, irritative cough,** and **colic.** Anhalonium tincture in drop doses has been claimed to be useful as a sustainer of the heart action. But little knowledge of its clinical value in circulatory disorders has as yet, however, been obtained. According to Landry, the drug is a useful adjuvant to digitalis.

The taste of the liquid preparations of anhalonium is bitter and unpleasant, but can readily be disguised. Lewin recommended for this purpose the use of fluid-extract of licorice and elixir of yerba santa (fluidextractum eriodictyi). The powdered drug may be administered in capsules or cachets.

The chief untoward action to be feared in the event of excessive dosage of this drug is respiratory depression.   S.

ANHIDROSIS, or ANIDROSIS.
See Sweat Glands, Diseases of.

ANIMAL EXTRACTS, OR ORGANOTHERAPY.—Owing

mainly to the fact that physiologists even at the present writing (1921) have failed to discover the functions of any ductless gland, despite considerable effort to do so, empiricism still prevails to a very large extent. Textbooks of therapeutics and practice still adhere to the convenient statements that an organic prepara-

tion "is useful," that "it is recommended," or "has proven valuable" in this or that disease; that is to say, without attempting to define its mode of action. The cause of this is not difficult to find: So many assumptions as to the actual functions of the organs used therapeutically have been vouchsafed on totally inadequate experimental evidence that textbook authors adopt none.

The writer of the present article has taken another course. Rejecting all assumptions based on inadequate data, he has done his own experimental work and used data from *all* branches of medicine, clinical and auxiliary, as a foundation for his own deductions. Time has sanctioned this course. The conclusions he published in the earlier editions of his "Internal Secretions," and elsewhere, have steadily gained adherents, supported as they have been by an increasing number of confirmatory facts contributed independently by experimenters and clinicians. He feels it his duty, therefore, to adopt his own views as the foundation of the summary of organotherapy submitted, knowing that they will best subserve the interests of the practitioner.

The human body is managed by the endocrine glands of the body. Every individual from the time he is born until the time he dies is under the influence of these many different kinds of elements—some of them having to do with the development of the bones and teeth, some with the development of the body and nervous system, some with the development of the mind, etc., and, later on—with the introduction of sex features—with reproduction. Still later on, these elements have to do with the preservation of these structures and functions which constitute the

body and mind, and if these glands become under- or over- active there is a disturbance of the specific functions which these component parts are supposed to perform; and since these glands are dependent on each other, the upset of one disturbs the rhythmical action of the others.

In recent years our knowledge as to the physiology of the ductless glands has been put to the test by endocrine therapy, and there is no longer any doubt that the future of medicine lies along these lines. In the writer's practice, endocrine therapy has displayed and replaced the old time drugs, so that practically 90 per cent. of all prescriptions for internal use consist almost entirely, if not wholly, of endocrine extracts. The varying forms of amenorrhea, most of the menorrhagias and metrorrhagias, threatened miscarriage, habitual miscarriage, sterility, the disorders and disturbances of the climacterium, and many other states met with in gynecological practice may be corrected in many instances specifically by a certain extract; in many other cases, by a combination of extracts. S. W. Bandler (Med. Record, Mar. 15, 1919).

Instead of using the extracts of organs the venous blood issuing from the organ should be used. This contains the true internal secretion while the cells of the organ cease secreting this product when they are dead. Hence the removal of the organ from the body to make the extract not only arrests production of the internal secretion but probably modifies essentially the delicate secretion already on hand in the tissues of the organ. Instead of a living secretion only a dead and possibly decomposed product is obtained. The efferent blood contains the secretion in its maximum vital potency. In 1911 the writer published researches on the thyroid secretion thus obtained in the efferent blood, and in 1913 and 1915 similar researches on the venous blood from the suprarenals, pancreas, and testicles. Man-

fredi announced in 1913 that the efferent blood from the pancreas inhibited certain actions of epinephrin. He cites further researches since by Ollini, Masera, Durand and 8 others. The difficulty in obtaining the efferent blood or lymph hampers and limits the research in this line, but this should be the goal toward which we strive. G. Ghedini (Jour. Amer. Med. Assoc., from Gaz. degli Osped. e delle Clin., Jan. 5, 1919).

Clinical, anatomic, histologic and bacteriologic observations led the writer to conclude as follows: The absence of certain accessory food factors from the dietary—improperly termed "antineuritic"—leads not only to functional and degenerative changes in the central nervous system, but to similar changes in every organ and tissue of the body. The morbid state to which their absence gives rise is not a neuritis. The symptom complex resulting from the absence of these substances is due (a) to a chronic inanition; (b) to derangement of function of the organs of digestion and assimilation; (c) to disordered endocrine function; (d) to malnutrition of the nervous system, and (e) to hypersuprarenalinemia. Certain organs undergo hypertrophy; others atrophy. Edema has invariably (100 per cent.) been associated with great hypertrophy of the suprarenal glands, while 85 per cent. of all patients having great amount of epinephrin in such patients as determined by physiologic methods, has been considerably in excess of that found in normal suprarenals. Inanition gives rise to a similar state of suprarenal hypertrophy, and to a similar state of atrophy of other organs, the brain excepted. The edema of inanition and of beriberi is believed to be initiated by the increased intracapillary pressure which results from the increased production of epinephrin, acting in association with malnutrition of the tissues. R. McCarrison (Brit. Med. Jour., Feb. 15, 1919).

Since the internal secretions and their hormones have been definitely

connected with the general protective mechanism of the body, they form the systemic immunizing mechanism of the organism. In reaching this conclusion so pregnant with probabilities that internal medicine as a whole will be completely revolutionized, Sajous, for more than a score of years, has by his conscientious labors, analysis of all reliable data derived from all sources—medical and auxiliary—and from coördinated syntheses of all factors entering into the problems, reached conclusions which have filled many obscure *lacunæ*, and bid fair to make a logical whole of what now, in medicine, is decidedly chaotic. While these hormones are the active defensive agents and their efficiency controlled by pharmaco-endocrinology, yet it may be that these same hormones may so increase the proteolytic activity of the digestive enzymes (defensive ferments) as to cause them not only to destroy pathogenic agents, bacteria, toxins, and certain other poisons, but also the blood cells (hemolysis) and even the tissues themselves (autolysis).

The recognition of this long continued and constructive work has been recognized by the establishment of a chair of endocrinology at the University of Pennsylvania, where he, as professor, with additional facilities, may continue to add to the resources of scientific medicine. Reynold Webb Wilcox (The Medical Times, Jan., 1922).

THYROID GLAND ORGANO-THERAPY.—In the latter part of the last century, King, of London, showed experimentally that the colloid substance of the thyroid gland passed directly into the lymphatics. Schiff, of the University of Geneva, reviving views in 1859 previously held by many, found that this organ played an important part in the economy, through some substance which it secreted, and that intraperitoneal transplantation of the healthy gland in a dog shortly after thyroidectomy had been performed prevented the cachexia strumipriva and violent nervous phenomena which follow this operation. Then followed, in 1882, the labors of the brothers Reverdin, succeeded, in turn, one year later by those of Kocher, of Berne, demonstrating that, in man as well as in animals, the same phenomena occurred under identical circumstances.

The principal postoperative symptoms noted were: marked weakness and fatigue; a sensation of cold, pallor, hardness, and dryness; edematous swelling, thickening of the skin, and loss of hair, all with, as nervous phenomena: muscular stiffness and pains; tetany, sometimes attaining the violence of true tetanus, and even clonic convulsions. The brothers Reverdin termed this condition *postoperative myxedema* while Kocher called it *cachexia strumipriva*.

The thyroid gland *per se* was subsequently found to be responsible only for the myxedematous symptoms, however. The two external parathyroids, discovered in 1880 by a Swedish physician, Sandström, and the two internal parathyroids, discovered by a French physician, Nicolas, of Nancy, in 1893, and independently by Kohn, of Prague, in 1895, were subsequently shown through the labors of Gley, Vassale and Generali, Moussous, Jeandelize, and others to be responsible for the nervous phenomena, tetany, etc. Briefly, removal of the thyroid alone arrested development and caused myxedema (cretinism in the young), while removal of the parathyroids alone was followed by tetany and early postoperative death.

The observation of Schiff, con-

firmed by other investigators, that grafting prevented the morbid effects of thyroidectomy as long as the grafts lived, led Murray and Ord to try the use of thyroid extract in myxedema. Not only was it found to counteract this disease by these clinicians and many others since, but thyroid gland, which includes parathyroid; but the latter alone, as will be shown under a special heading, also proved valuable therapeutically in other disorders.

How are these favorable phenomena brought about?

PHYSIOLOGICAL ACTION.— In a recently published work on general therapeutics, one of the contributors states that: "the manner in which the thyroid gland presides over the nutrition of the body is unknown. It is generally admitted that it furnishes an internal secretion, that this secretion is formed by the living cells of the vesicles, and that it is poured into the colloid material they contain. But our knowledge," remarks the author, "has not advanced much beyond this point." This naturally suggests a corresponding lack of knowledge concerning the physiological action of thyroid preparations and their use as remedies. But here, as elsewhere in the realm of science, the world has not stood still.

In truth, the last three decades have brought out facts which account not only for the nutritional phenomena witnessed under the influence of thyroid preparations, however administered, but also for autoprotective or immunizing functions of the first order.

ACTION ON METABOLISM.— Some physiologists hold that the thyroid and parathyroids, by means of an internal secretion, "exercise an important control over the processes of nutrition of the body," as Howell states; others contend that the purpose of these organs "is to neutralize or destroy toxic substances formed in the metabolism of the rest of the body." Others again assert that it increases metabolic activity, especially catabolism. The one great factor which stays all progress in this connection is the persistent identification of these functions as separate entities, whereas they are in reality the manifestations of a single function. That such is the case is easily demonstrable: No one can deny that "the processes of nutrition of the body" represent a phase (that of anabolism) of the process of metabolism, nor can any one deny that catabolism, the other phase of metabolism, serves to "neutralize or destroy toxic substances" formed in the body at large—and to break down fats, as is well known. If, therefore, *the thyroid secretion serves to activate metabolism,* as first shown by two Italian scientists, Vassale and Generali, all the other processes mentioned are also influenced by the thyroid. That such is the case has now been conclusively shown.

[Chantemesse and Marie, Ballet and Enriques (cited by Popoff, Arch gén. de méd., Oct., 1899), Bourneville (Arch. de neurol., Sept., 1896), and Shattuck (Boston Med. and Surg. Jour., June 30, 1904), Lorand (Lancet, Nov. 9, 1907), and many other clinicians, including myself, have noted that thyroid preparations caused a rise of temperature of several degrees and that it took part in the febrile process. These observations were controlled by those of Stüve and Thiele and Nehring (Zeit. f. klin. Med., xxx, p. 41, 1896), that thyroid extract increases over 20 per cent. the oxygen intake and to nearly as great a degree the carbonic acid output. This is evidently produced by the active agent of the thyroid secretion, iodine, for this halogen itself increases oxidation as well.

Thus, Rabuteau, Milanese, and Bouchard (C.-r. de la Soc. de Biol., pp. 227, 237, 1873), Henrijean, and Corin (Arch. de pharmacodyn., ii, 1896) have all noted an increase of nitrogen excretion. Wood ("Therapeutics," 13th ed., p. 499, 1906) and Cushny ("Pharmacology and Therapeutics, 4th ed., p. 514, 1906) state, in fact, that iodine can produce fever.

Removal of the thyroid, on the other hand, lowers oxidation. Albertoni and Tizzoni and Magnus Levy (Zeit. f. klin. Med., xxxiii, p. 269, 1897) found, for example, that this procedure decreased markedly the output of carbon dioxide, and that it caused hypothermia. The fall of temperature is gradual, according to Lorrain-Smith (Jour. of Physiol., xvi, p. 378, 1894), and most marked, according to Rouxeau (Arch. de physiol., xxix, p. 136, 1897), at the end of the operation. The proportion of red corpuscles is reduced, according to Moussu (C. r. de la Soc. de biol., p. 772, 1903). Reverdin observed in man that the hemoglobin was also diminished, while Horsley noted increased sensitiveness to cold. Albertoni and Tizzoni and Masoin found that the blood contained less oxygen than normally.

This applies as well to removal of the parathyroids, which was found by Jeandelize ("Insuffiance thyroidenne et parathyroidienne," p. 45, 1903) also to lower the temperature. That the thyroid apparatus can itself raise the temperature, is shown by the febrile process and sense of heat with flushing observed in the sthenic stage of exophthalmic goiter and when the thyroid apparatus is overactive when thyroid extract is given to such cases, the exchanges may be increased to a surprising degree—77 per cent. in a case observed by Hirschlaff (Zeit. f. klin. Med., xxxvi, No. 3-4, S. 200, 1898-99). The last two decades have only served to confirm these observations. C. E. DE M. S.]

As urged by myself in 1903, the thyroid enhances general oxidation and metabolism is partly due to excitation of the adrenals by the thyroid secretion contained in the blood. Starling has since (1906) termed "hormones" substances which thus act as stimuli to other organs, while Kraus and Friedenthal, Caro, Hoskins, and others have found (1908-1910) that thyroid extracts excited the adrenals. In addition to this, I attributed (1907) to the thyroparathyroid principle a direct action on the phosphorus of all tissue-cells (and particularly of their nuclei), the iodine found by Baumann to be the active agent, in organic combination, of the thyroid secretion (as well as of the parathyroids, as shown by Gley), rendering the phosphorus more susceptible to oxidation by the hemoglobin.

[Telford Smith (Lancet, Oct. 7, 1897) and other clinicians have observed that the use of thyroid preparations in young cretins was sometimes attended by softening of the bones and bending of the legs, notwithstanding marked general improvement. When it is recalled that five-sixths of the inorganic matter of bone consists of calcium phosphate, it becomes a question whether the thyroid extract does not interfere with the building up of this tissue. That such is the case is further suggested by the facts that iodine, the active constituent of the thyroid secretion, and its salts, as shown by Henrijean and Corin (loc. cit.), Handfield Jones (cited by Wood, loc. cit.), and others, cause excessive elimination of phosphates and phosphoric acid, and that thyroid preparations, according to Roos, Scholtz, (Central. f. inn. Med., xvi, pp. 1041, 1069, 1895), Pouchet (Bull. gén. de thérap., Sept. 15, 1905), and others, act in the same way. "Emphasis must be laid," writes Chittenden (Trans. Congress Amer. Phys. and Surgs., iv, p. 93, 1897), "upon the apparent connection between the thyroid gland and phosphoric acid metabolism," giving as example "the increased excretion of P_2O_5 after feeding thyroids to normal animals, and the great decrease in the case of animals with the thyroids removed."

The untoward effects of large doses of thyroid preparations on the nervous system, owing to its wealth in phosphorus and fats as manifested by tremor, tachycardia, optic neuritis [Coppez (Arch.

d'Ophtal., Dec., 1900)], etc., also bespeaks such an action; Cyon (Arch. de physiol., x, p. 618, 1898), in fact, found that injections of iodothyrin excited the depressor nerve directly to such a degree that the vascular pressure often declined to two-thirds of the normal.

A familiar action of the thyroid preparations is a rapid reduction of fat in obese subjects when full doses are administered. The presence in the fat-cell of a nucleus rich in phosphorus whose purpose is promptly to promote oxidation of the fat when the organism requires additional carbohydrates explains this action. Schöndorff (Arch. f. d. ges. Physiol., lxiii, p. 423, 1896; lxxii, p. 395, 1897), in fact, found that the reserve fats could be exhausted before the nitrogenous tissues were affected.

The mode of action of the thyroid active principle, iodine, is suggested by the presence of this halogen in all nuclei, as shown by Justus (Virchow's Archiv, clxxvi, S. 1, 1904) and others. "If a fragment of phosphorus lying on a plate is sprinkled with iodine," writes Wilson ("Inorganic Chemistry," p. 284, 1897), "the substances unite, and heat enough is produced to kindle the phosphorus." Moreover, Roos (Münch med. Woch., No. 47, p. 1157, 1896) found that in a dog in nitrogenous equilibrium, iodothyrin "caused at once a marked increase in the output of sodium, sodium chloride, and phosphoric oxide" (cited by Chittenden, *loc. cit.*, p. 89).

The experimental observations of Notkin and White and Davies, and personal researches having suggested that the action of the adrenal secretion resembles that of an organized ferment, I termed it "thyroidase." C. E. de M. S.]

The writers, using dogs, tried to determine the value of small doses of commercial desiccated thyroid gland, given by mouth, as a means of increasing nitrogen elimination. To eliminate the determination of a nitrogen intake, the dogs were given only sugar solutions, and their nitrogen excretion, following the administration of the thyroid gland preparations, was carefully studied and tabulated. Examination of the tables presented, which show the average

nitrogen figures for 3 days preceding thyroid feeding and for the days of administration, and 2 days subsequent to it, indicate that a daily dose of 0.05 to 0.1 Gm. (¾ to 1½ grains) of desiccated thyroid mixture per kilo (2⅕ pounds) of body weight is sufficient to produce a marked effect on the nitrogen elimination, with a somewhat greater loss in weight than in the control animals. Rohde and Stockholm (Jour. of Biol. Chem., Feb., 1919).

When in the light above, we administer desiccated thyroid, which combines the actions of the thyroid and parathyroids, corresponding effects are produced: It renders the phosphorus of all tissues, and all free substances, such as bacteria, wastes, toxins, etc., containing phosphorus, more inflammable or sensitive to the action of the oxygen in the blood. As this applies particularly to nerves and nerve centers (all of which are especially rich in phosphorus), the adrenal center, and, therefore, the adrenals themselves, are excited, and, the adrenal secretion being the agent which takes up the oxygen of the air to sustain the blood-oxygenizing power, the supply of oxygen is also increased. All the various phosphorus-laden substances are thus not only rendered more readily oxidizable by thyroid extract, but this remedy also provides indirectly the required oxygen. Hence also the familiar influence of thyroid preparations on obesity, their action being mainly exercised upon the nucleus rich in phosphorus which fat-cells contain.

The wonderful effects of thyroid extract in cretinism can also be readily accounted for: The *rise of temperature* is due to the increased oxidation brought about by the thyroid and adrenal oxidizing substances acting jointly; the *enhanced metabolism* is a

normal result of the augmentation of general oxidization, while the *increased appetite* is due to the resulting greater demand for foodstuffs. The marked improvement in *general nutrition* and *strength* is a self-evident result of the assimilation of a greater proportion of food materials, and the *rapid growth* likewise. The *cerebrospinal system* is particularly influenced owing to its wealth in phosphorus; hence, the *development of intelligence*. All organs being the seat of active metabolic activity and nutrition, the intestinal, renal, cardiac, and cutaneous and hepatic functions are all enhanced. Even the hair grows, not only in cretinism, but when its loss is due to general adynamia.

> A slightly alkaline saline solution, or alcohol, extracts from the thyroid some non-coagulable material which is a vigorous stimulant for the gastric secretion. This material produces its effects at least in part by intensification of the functions performed by the terminal filaments of the (gastric) vagus. Extracts similarly made from the pathologic tissue of the adenomatous or hypertrophied human glands are inert. Rogers, Rahe and Ablahadian (Amer. Jour. Physiol., Feb. 1, 1919).

This, it must be emphasized, is the aggregate of effects obtained with *small* doses, at most, 1 grain of the desiccated thyroid (which represents 5 grains of the gland proper), three times a day. When larger doses are given another order of phenomena is awakened: those of excessive burning up, as it were, of the tissues. The inflammability of all phosphorus-laden elements being markedly enhanced while the quantity of oxidizing substance is as greatly increased, the tissue elements are broken down more rapidly than they are built up, beginning with the fats, and the patient becomes emaciated.

THYROXIN.—Until recently the iodothyrin of Roos was deemed the probable active agent of the thyroid secretion, but the recent more precise biochemical researches of Edward C. Kendall, of Rochester, Minn., (Endocrinology, April, 1917, and April-June, 1918), have identified it as a crystalline compound containing iodine. The colloid of the thyroid was not found, as generally believed, to influence the functions of the body at large. The crystalline compound referred to, "thyroxin," was found, even in small doses, to supplant thyroid activity, relieving myxedema and cretinism and in excess will produce symptoms of exophthalmic goiter. As little as 10 milligrams ($\frac{1}{6}$ grain) will, in fact, increase the metabolic rate 30 per cent. The name "thyroxin" is an abbreviation of "thyro-oxy-indol," the CO-NH group of which is thought to produce physiologic effects with iodine probably as an activator.

The exact chemical reactions involved, however, are still *sub judice* but it is theoretically attributed to an interaction between thyroxin and an amino-acid, the function of the thyroid from this viewpoint being to furnish the animal organism with ammonia resulting from the deaminization of amino-acids, leading perhaps to the formation of urea.

Antitoxic Function.—Another function definitely credited to the thyroid gland is "to neutralize or destroy toxic substances formed in the metabolism" (Howell). Now tetany, as shown by the brothers Reverdin, we have seen follows thyroidectomy; it is now recognized that this is due to a general toxemia. As these phenomena were arrested by administering thyroid extract, or by grafting, as long as the physiological action of these remedial agents lasted, it became evident that the thyroid supplied the blood with some substance which in some way destroyed the spasmogenic poison, *i.e.,* that the thyroid product was an antitoxic substance. This is further sustained by the facts: 1, that the blood

of thyroidectomized animals proved more toxic than that of normal animals, and that it caused convulsions; 2, that the urine of thyroidectomized animals was also more toxic than that of normal animals; 3, that the transfusion of blood of the latter into thyroidectomized animals counteracted for a time the toxicity of both their blood and urine. These and other facts had shown that the thyroid gland—mainly owing to the parathyroid secretion it contains—is endowed with antitoxic, or, as they have been sometimes termed, "detoxicatory," functions.

Yes; it is evidently not only "toxic substances formed in the metabolism of the body" that the thyroparathyroid secretion proves antitoxic. Charrin, Lindemann, and others have found, for example, that animals succumbed more readily to infections after their thyroid had been removed; Roger and Garnier, Kashiwamura, and others found that histologically the thyroid showed evidences of marked activity, while Torri noted that this was accompanied by an increased production of their colloid substance. Hunt has shown that thyroid feeding renders white mice much less susceptible to poisoning by acetonitrile; Vincent, Frugoni and Grixoni, Léopold-Lévi and Rothschild, and others have observed that thyroid preparations combated effectively various infectious diseases, including erysipelas and septicemia. The thyroparathyroid thus showed itself antagonistic to bacterial toxins and certain other poisons, as well as to toxic waste products.

This action is accounted for by the fact, pointed out by myself in 1903 ("Internal Secretions," vol. i), that the thyroid secretion is one of the important agents *in general immunity*—none of the active factors or antibodies of

which had been traced to their source. I found, however, that this action was indirect, *i.e.,* that the thyroid secretion or extracts, while a constituent of the blood's antitoxin, or alexin, increased the immunizing power of the latter by enhancing the functional activity of the adrenals. This stimulating influence on the adrenals has since been sustained by the investigations of Hoskins and others experimentally, while the participation of the thyroid in the immunizing process was, four years later, confirmed by the researches of L. Fassin, of the Bacteriological Institute of Liége.

Experiments to ascertain the influence of the thyroid gland on immunity. The first series of experiments in a large number of animals (dogs and rabbits) showed that the subcutaneous injection of thyroid product (fluidextract of the fresh gland, the thyroidin of Burroughs, Wellcome & Co.) is rapidly followed by an increase of alexin in the serum, a substance discovered by Buchner, generally considered as playing an important rôle in the defense of the body. This increase becomes evident as early as ten minutes after the injection; it becomes accentuated after one hour, reaches its maximum in twenty-four hours; then the proportion of alexin in the blood recedes more or less rapidly until the normal is reached. The effects of one injection rarely last less than twenty-four hours or more than two or three days. The writer also found that the oral administration of thyroid brought about corresponding effects.

To control these results as to their direct relationship with the thyroid, the writer performed complete thyroidectomy in 9 animals. One alone, however, survived the operation more than fifteen days, tetany occurring in all, thus showing that the parathyroids had been completely removed. In all the operated animals there occurred a marked diminution of the hemolytic and bactericidal alexin, though it never d'sappeared

altogether. As the diminution of alexin might possibly have been due to traumatism, the operative procedures were repeated in fresh animals, leaving the thyroid *in situ*. But neither the traumatism nor even removal of the spleen caused a reduction of alexin. Louise Fassin (C.-r. de la Soc. de Biol., vol. lxii, pp. 388, 467, 647, 1907).

Further researches on the nature of the process through which the thyroid secretion enhanced the autoprotective power of the blood and of the phagocytic activity of the migrating and stationary (endothelial) cells brought me in 1907 to the conclusion that the thyroid and parathyroid secretions, acting jointly, served to sensitize all phosphorus-laden cells, normal and pathological, and that this thyroparathyroid secretion and Wright's opsonin were "one and the same substance." Among the more direct facts which sustained this opinion were that, while substances capable, as are the opsonins, of sensitizing or enhancing the phagocytic activity of leucocytes had been found in the blood-plasma by Denys and Leclef, Bordet, and others, and Nolf had shown that they were secreted by the red corpuscles, my own observations brought out (1) that the composition of these sensitizing substances was similar to that of the thyroparathyroid secretion, *i.e.*, that they contained iodine, nucleoproteid, and globulin, and (2) that opsonins, which had been assimilated to Bordet's sensitizing substance by Savtchenko and others, were destroyed at the same temperature as the thyroparathyroid secretion, *i.e.*, at 60° to 65° C. Briefly, besides being endowed with other attributes in common, the sensitizing substances of Denys, Bordet, etc.; Wright's opsonins, and the thyroparathyroid secretion all proved to be plasmatic products of the

red corpuscles, and to show similar chemical properties. Hence my conclusion that it was as opsonin that the thyroparathyroid secretion produced its main effects, and the recommendation that thyroparathyroid preparations be used in various infections, acute and chronic, to enhance the opsonic power of the blood. My position has been sustained by several investigators.

The writer reported the results of experimental and clinical observations which had led him to conclude that the opsonins of the tissue juices and exudates were, to a considerable extent, the product of the thyroid gland while simultaneously taking part in the maintenance of health through its influence on metabolism. He noted elevation of the opsonic index of the serum after injections of thyroid extract into rabbits. A rabbit treated with 1.5 c.c. of the extract at two days' interval gave three days after the injection an opsonic index = 2, 4, for example. Another, given the preceding day 1 c.c. of the extract, gave an index of = 3.0. These results, obtained in many animals, and other experiments led the writer also to ascribe the opsonizing action of thyroid extract to the thyroglobulin of Oswald, which is normally present in the thyroid gland. Stepanoff (C.-r. de la Soc. de Biol., vol. lxvi, p. 296, 1909).

The writer, having also advanced the opinion that the glands with internal secretion probably play an important rôle in the phenomena of immunity, undertook to verify this view experimentally, as had Stepanoff, at the Pasteur Institute. The first series of experiments aimed to ascertain the influence of hyperthyroidization on opsonic variations in the blood of guinea-pigs and rabbits, using mainly the bacilli of tuberculosis, diphtheria, the *Bacillus coli,* and the staphylococcus and streptococcus. A large dose of thyroid (1 Gm. per kilo) was given the first day, but this was reduced daily. In this series, which included 116 examina-

tions, the writer states that he always observed that the opsonic power of the blood-serum increased very clearly after thyroid opotherapy. It was, in fact, considerably more than doubled in all but one instance, the exception being that of an animal in which an emulsion of *Bacillus coli* only increased the opsonic power one-half.

Might the ingestion of any animal substance by herbivora not have given rise to the increase of opsonic activity? The administration of corresponding quantities of horse flesh to control failed to modify the latter in any way. The writer found, moreover, that the leucocytes of a normal animal when treated *in vitro* with the serum of an hyperthyroided animal showed a distinct increase of phagocytic activity.

The second series of experiments had for its purpose to ascertain the effects of removal of the thyroid on the opsonic properties of the blood. The serum obtained from 4 dogs at the time of the characteristic accidents caused by thyroidectomy showed in every instance a most evident diminution of opsonic power. The same experiments conducted in the rabbit gave rise to the same results, *i.e.*, he always found a marked decline of opsonic power in thyroidectomized animals. He noted, moreover, that, while traumatism, even a musculocutaneous wound, could cause in a certain measure a reduction of opsonic power, the latter rapidly returns to normal, while it maintains itself a very long time at the same level in thyroidectomized animals. S. Marbé (C.-r. de la Soc. de Biol., vol. lxiv, p. 1058, 1908).

Briefly (see the present, 1922, status of the question by R. W. Wilcox, pages 688 and 689), the physiological action of thyroid preparations may be summarized as follows:—

1. They enhance oxidation by increasing the inflammability of the phosphorus, which all cells, particularly their nuclei, contain, and by enhancing the functional activity of the adrenals.

2. Their power to enhance the inflammability of cellular phosphorus extends to pathogenic elements, bacteria, their toxins or endotoxins, toxic wastes, etc. As such they act as opsonins, and render these pathogenic elements vulnerable to the immunizing action of the blood and its phagocytes.

THE ACTIVE PRINCIPLE OF THYROID.—The thyroid product is an "iodized globulin." As Notkin and also White and Davies hold, the action of the thyroid secretion resembles that of an organized ferment. This finds its explanation in the fact that the thyroidin, to which this applies, is mainly a ferment *plus* iodine. The identity of this ferment suggests itself when we consider Baumann's analyses of his thyroidin. Among other tests, for example, he found that it was practically insoluble in ether and chloroform; that it was not destroyed by digestive ferments, and that it stood a temperature of 100° C. These are the specific tests of the oxygen-laden adrenal product, my adrenoxidase. Again, I found that this substance gave the tests of the plasmatic oxidase; Lépinois also found that the thyroid secretion contained an oxidase which gave the blue reaction with tincture of guaiac. We have seen, moreover, that adrenoxidase is a globulin: Oswald termed his product "thyroglobulin" and described it as an "iodized globulin."

The recent discovery of Kendall of crystalline body in the thyroid, he termed "thyroxin" has already been reviewed on page 693, and its possible rôle in metabolism described.

The crystalline body containing over 60 per cent. of iodine prepared from the thyroid by Kendall, of the Mayo Clinic, was tried on cretins and

myxedema patients. The results justify the view that this substance is to be regarded as a hormone having the functions ascribed to the thyroid. They very definitely indicated that a gain, not a loss, of nitrogen is a result of the therapeutic action of thyroid; and *vice versa,* that a loss of nitrogen, that is, protein, is due to a toxic condition of the gland. They showed also that usually too great an amount of thyroid is prescribed in hypothyroidism. The thyroid of obesity depends on a toxic effect, as it is accompanied by nitrogen loss. It should therefore be discouraged. N. W. Janney (Arch. Internal Med., xxii, 187, 1918).

PREPARATIONS AND DOSE.
—The implantation of a portion of the thyroid gland beneath the skin was soon superseded by the hypodermic method, but the latter presented another drawback, that of requiring the constant attendance of the physician. Besides this the preparations often produced suppuration. The gland itself, therefore, administered in the form of desiccated powder in tablets or capsules, is preferred by the majority of practitioners. This presents also the advantage of conforming to the Ninth Decennial U. S. Pharmacopœia (*thyroideum siccum*) made official from September 1, 1916.

The average dose recommended in the previous Pharmacopœia was entirely too large, but this was corrected in the last edition. It is now $1\frac{1}{2}$ grains (0.1 Gm.).

But much smaller doses $\frac{1}{4}$ grain and even less, three times daily may be advantageously used, even in the adult. While small doses enhance metabolism, larger doses so stimulate catabolism that they cause undue breaking down of the fats and tissues.

If kept up too long, the blood ele-

ments themselves (hemolysis), and even the tissues (autolysis) proper, may be destroyed. Five- or even 4-grain doses—the former dose of the U. S. P.—are never indicated, even in the treatment of obesity.

By loading up the circulation with toxic wastes, these excessive doses may also give rise to tetanoid movements and even to true tetany.

An important feature in this connection, however, is that the preparations of desiccated thyroid on the market vary in strength to a considerable degree, and that a small dose of a weak preparation may prove practically inert in practice. This is due to the fact that they have not as yet been standardized. This does not apply to an imported desiccated thyroid, that of Burroughs, Wellcome and Co., which is standardized, each grain (representing about 6 grains of the fresh gland) containing 0.02 of iodine in organic combination. It is upon this standard that the dosage recommended above is based. It is available in small tablets of $\frac{1}{4}$, $\frac{1}{2}$, 1, $1\frac{1}{2}$, $2\frac{1}{2}$, and 5 grains.

There is also on the market an imported article termed *iodothyrin,* a milk-sugar triturate of the thyroid active principle, 1 Gm. of which represents 0.0003 Gm. of iodine. The dose for adults is given as 10 to 30 grs. (0.6 to 2 Gm.), and is available in tablet form, each containing 5 grains (0.33 Gm.) of iodothyrin. Its manufacturers claim that, besides possessing the advantage of definite strength, it is devoid of extraneous matter. It is not regarded as efficacious as the desiccated gland. It is a convenient preparation for young children, however, owing to the fact that it occurs as a sweet, whitish powder.

When preparations of thyroid gland —which include parathyroid—cannot be obtained, a *glycerin extract* may be prepared by divesting a sheep's gland of fat, and macerating it in an equal quantity in weight of glycerin twenty-four hours. From 2 to 15 minims of the extract may be given daily according to age.

> **Thyroxin** was found to have a definite therapeutic effect in **cretinism**, improvement in the clinical symptoms and a gain in nitrogen retention resulting. The optional daily dose was found to be 0.25 mg. ($\frac{1}{250}$ grain) hormone iodine, representing approximately 0.75 mg. ($\frac{1}{80}$ grain) thyroxin, and corresponding to 4 grains (0.26 Gm.) of thyroid tablets. It could thus be demonstrated that as a rule too great an amount of thyroid is prescribed in hypothyroidism. Janney (Arch. of Internal Med., xxii, 187, 1918).

UNTOWARD EFFECTS AND THEIR PREVENTION.—The dangers attending the use of thyroid preparations depend, to a degree, upon the manner in which the remedy is administered. Beneficial doses, by raising the activity of all metabolic processes, prove tonic, increase the appetite, the strength, and the oxidations, as shown by a slight rise in temperature. When, however, the dose is too large, a weak, rapid pulse and shortness of breath, vomiting, cardiac oppression, a feeling of tightness around the chest, vertigo, and coma may supervene. Excessive doses have also caused anorexia, diarrhea, malaise, lassitude, and pain in the extremities; headache, various eruptions, urticaria, transient and papular erythema and eczema, and, in some cases, nervous manifestations; neuralgia, delirium, convulsions, delirium of persecution, aphasia, monoplegia, etc. When dried powder or compressed tablets that are not fresh are used, symptoms of ptomaine poisoning may be added to those mentioned. Hence, the observations that these preparations are more likely to produce such effects during the warm weather.

The best guide is the pulse. Any considerable quickening or palpitation should lead us to discontinue the drug until the cardiac action is again normal. There are no dangers in the use of the drug, provided we begin with small doses, from $\frac{1}{4}$ to 1 grain, and gradually increase, watching the pulse. It should never be given to a patient who cannot be closely watched.

In some cases, although no other untoward symptom appears, the patient loses flesh. This is apt to occur when 2 grains of the dried gland three times daily in the adult is exceeded.

Chronic poisoning, characterized by rapid pulse, emaciation, weakness of the limbs, general debility, and mydriasis have also been observed in individuals who had undertaken, without medical advice, to treat their corpulency, and who had, therefore, subjected themselves to excessive doses.

TREATMENT OF THYROID POISONING.—As a rule, cessation of the use of thyroid preparations arrests the untoward effects. When such is not the case, however, **arsenic,** as shown by Mabille, antagonizes the toxic phenomena. Fowler's solution, from $3\frac{1}{2}$ to 5 drops three times daily, suffices in most instances to arrest all morbid effects.

Mabille's observation that **arsenic** obviates the unpleasant symptoms excited by thyroid preparations were confirmed by Ewald. In 5 cases of idiopathic goiter, in 1 case of obesity, and 1 of infantile myxedema, iodothyrin was given in progressive doses of from $3\frac{1}{5}$ to 30 or $38\frac{1}{2}$ grains daily. At the same time arsenic

was given, either in pills or as Fowler's solution, in doses increasing proportionately to the iodothyrin of $\frac{1}{64}$ to $\frac{1}{10}$ or even $\frac{1}{8}$ grain daily.

Although the 7 cases took respectively 231, 111, 86, 320, 108, 296, and 125 iodothyrin tabloids, containing nearly 4 grains each, beyond occasional increased frequency of the pulse no symptoms of thyroidism appeared, so that the course could be continued uninterruptedly. Arsenic, therefore, appears to suppress thyroidism with greater certainty than atropine does iodism, and it is possible to give iodothyrin safely in doses and for a period capable of producing definite therapeutic effects.

The addition of a cardiac tonic, preferably **adonidin**, to thyroid is recommended whenever the latter preparation is to be used for any length of time. The following formula is employed:—

R Sodium cacodylate .... $\frac{1}{200}$ gr.
  Adonidin .... $\frac{1}{30}$ gr.
  Thyroid gland (dry powder). 1 gr.

For 1 compressed tablet. When fresh adonidin cannot be obtained (its price is exceedingly high), **caffeine** may be substituted in doses of $\frac{1}{6}$ grain. Thyroid therapy will receive a new stimulus as soon as the medical profession appreciates the fact that the addition to the thyroid of proper amounts of arsenic and a cardiac remedy will render the medication more efficient and deprive it of all or nearly all its deleterious effects. Heinrich Stern (American Medicine, Jan., 1910).

THERAPEUTICS.—The many disorders in which thyroid preparations have been recommended ("nearly all the chronic and many of the acute troubles known to humanity," as one author remarks) have naturally inspired considerable mistrust as to their actual therapeutic value. Gradually, as the harmfulness of large doses asserted itself and the physiological rôle of the thyroparathyroid apparatus became unraveled, however, their indications became better defined. It may now be said that in sharp contrast with the empirical methods of the past thyroid preparations, when employed intelligently, are of great value in many disorders, both acute and chronic, mainly through their potent influence over metabolism due to the contained organic iodine. Recent experimental and clinical investigations have well shown that the thyroid acts more powerfully in accelerating metabolism than any other known agency.

The writer's experiments emphasize the extraordinary affinity of the thyroid tissue for iodine. As high as 18.5 per cent. of a given intake of iodine by mouth may be recovered from a thyroid whose ratio to the body weight is as 1:687. Again, maximum thyroid effects may be induced by minimum amounts of iodine. The amount of a given intake absorbed depends, for the most part, on the size of gland and the existing degree of hyperplasia or the degree of saturation with iodine at the time of its administration. Marine (Jour. Biol. Chem., Oct., 1915).

Basal Metabolism.—This method of ascertaining the degree of activity of the thyroid gland has recently received considerable experimental and clinical support.

As it is reviewed under Graves's disease, it may be recalled that while the basal metabolism of a normal individual varies but about 10 per cent., any greater variation is of endocrine origin, the thyroid furnishing the widest variations.

The writer found in a case of exophthalmic goiter that the standard of metabolism reached 80 per cent. above normal, and in a myxedema patient 40 per cent. below normal. Krogh (Ugeskrift f. Laeger, Dec. 29, 1916).

In the light of the functions attributed to the thyroid secretion in the foregoing pages, it governs tissue metabolism by rendering all phosphorus-laden cells susceptible to oxidation. When, therefore, the thyroid principle is deficient in the body, both phases of metabolism—including, of course, that of carbohydrates—the building up and the breaking down of tissues, are correspondingly inhibited. The most exaggerated expressions of this condition are, as is well known, the syndromes known as myxedema and cretinism. The characteristic symptoms of these disorders exemplify clearly deficient metabolic activity and its consequences. In myxedema we have, among other symptoms, for example, the low temperature, 95.5° F. in some instances, both in the mouth and rectum; great sensitiveness to cold, reduction of the urea output—sometimes to 50 per cent. of the normal—cyanosis of the lips, ears, and extremities on exposure to slight cold, and many secondary results of deficient metabolic activity, anemia with marked pallor, general relaxation of the arteries, muscular weakness, mental torpor and vertigo, and the cutaneous anesthesia. In the cretin, we have, besides, all the phenomena of arrested development, both physical and mental, as shown by the dwarfed body and the idiocy.

Hypothyroidia, or Hypothyroidism.—This is a condition akin to the above, but much less marked, frequently met in practice. The thyroid apparatus supplies a part only of that required by the tissues, and the resulting phenomena recall closely some of those observed both in myxedema and cretinism: chilliness and subnormal temperature, coldness of the extremities and sensitiveness to cold; fatigue on slight exertion; constipation with tendency to tenesmus; frequent attacks of migraine, "sick headaches" with nausea, vomiting, etc., and other periodic manifestations of autointoxication—due to inadequate reduction of waste products and their retention in the blood. The skin taking part in the process of elimination, urticaria and eczema are frequently observed, while transitory edemas of the brow, around the eyes, and sometimes of the face, even in the absence of albuminuria or casts, point to renal fatigue. Enuresis is commonly observed in children of this type and may persist to adult age. The patient is subject to frequent catarrhal disorders of the respiratory passages, usually ascribed to colds, but due mainly to vascular and glandular relaxation. A tendency to early alopecia, including the eyebrows (especially the outer third), is also noticeable—a sign of deficient general nutrition which coincides with a marked proclivity to early senility.

In women the menstruation appears late, owing to retarded development, and there is a proclivity to metrorrhagia due to laxity of the muscular coats of the uterine arterioles, while pelvic disorders are apt to occur owing to deficient support of the uterus, lack of tone in its muscular elements. Leucorrhea is also frequent, owing to relaxation of the glandular elements of the whole genital tract. Such women conceive readily, but abortion is very frequent among them; if the fetus is carried to the normal period, they have little or no milk. Children born of such mothers make up the largest number, if not all, the cases of cretinism, rickets, harelip, cleft palate, and other malformations usually ascribed

to hereditary influence. We are dealing simply with deficiency of the iodine in organic combination which the thyroparathyroid glands supply to the organism to sustain their intrinsic metabolism, *i.e.,* their vital activity.

Hertoghe has urged the importance of the maternal thyroid on the development of the fetus, hypothyroidia from fault be added tuberculosis, hereditary syphilis, alcoholism, inanition, saturnism, or diabetes, the child will show undoubted signs of these taints, and will probably be a myxedematous cretin, with signs of rickets and achondroplasia, and to this cause may be assigned such malformations as harelip, cleft palate, bony deformities, hypospadias, or undescended testicle. Should the maternal taint be but slight, the child

Adipositas (8 months old). Weighs 36 pounds. (*Sheffield.*)

any cause favoring cretinism in the child. It also promotes sterility, the use of thyroid gland being often followed by pregnancy.

Hypothyroidia is often the cause of obesity in children, as well as in adults (see annexed cuts), and of the cold feet and hands and other phenomena observed in fat, pasty children.

> If the mother has at her disposal sufficient store of thyroid secretion, the child does well; but if there is **thyroid insufficiency,** and especially if to this

will merely be very backward, which is a matter of small amount in boys, and if after a time righted by the thyroid equilibrium being established; but in girls menstruation is late in being established; uterine retroflexion is frequent; the chest is undeveloped.

The author has often seen women nearing 40 years of age who are fat and whose menstrual flow is excessive take thyroid extract in order to reduce their **obesity.** He has often seen the menstrual flow in these women become modified, their stoutness decrease, and the women find themselves pregnant,

when they had for a long time given up all hope of ever being so again. He has often by means of thyroid extract brought to a successful end a **pregnancy** in women who have repeatedly miscarried. It is often noticed that in adults incontinence of the urine can be stopped by rest in bed. This comes about from the fact that, while resting in bed, the patient is subject-

artificial feeding, these signs become more pronounced, with eczema, urticaria, tardy dentition, etc. It seems evident that nurslings receive in mother's milk some of the products of the mother's thyroid functioning. The physiological hypothyroidism of the newborn may assume pathological proportions; any derangement in thyroid functioning on the part of the mother

Adipositas. Same case, back view. (*Sheffield.*)

ing his tissues to large doses of thyroid secretion. In the case of a pregnant woman the increase of thyroid secretion often becomes excessive during the pregnancy, and the woman suffers from the symptoms of excessive thyroid secretion. Hertoghe (Bull. de l'Acad. Royale de Méd. Belgique, April 27, 1907).

Thyroid insufficiency is the cause of many of the phenomena noted in young infants, such as a tendency to obesity, to transient edema, cold feet and hands, scanty and brittle hair, vasomotor disturbances, vomiting, somnolency, and slight resistance to infections. With

or wet-nurse may lead to severe symptoms of hypothyroidism in the infant. In several instances in the writer's experience infants became myxedematous when the mothers had goiter. In other cases, the healthy infants of healthy parents became myxedematous when they had a wet-nurse with goiter. All these children were cured with thyroid treatment and change of nurse. Experimental research with goats has confirmed the actual occurrence of transmission of thyroid secretion by the placenta and in the milk. Concetti (Annales de méd. et chir. infantiles, Aug. 15, 1909).

The rudimentary forms of **myxedema** or **hypothyroidism in children** are particularly liable to escape recognition, while thyroid treatment in time is almost a certain cure. In a case of this kind a boy of 6 had not grown in the last two years, but seemed otherwise normal, although not particularly bright. Under cautious thyroid treatment by the end of eighteen months he had grown 11 cm., nearly 4½ inches. In 2 other cases the myxedema developed after severe measles or mumps, with acute thyroiditis in the latter case. The thyroid treatment ordered was soon abandoned by the family, and the child developed pronounced myxedema, but after two years it spontaneously subsided. In a fourth case the myxedema developed after a severe fall over a balustrade, the throat in front bleeding from the injury. Thyroid treatment promptly cured the child. "Pasty" children, fat, pale, and flabby, may be suffering from hypothyroidism and require thyroid treatment. Stoeltzner (Jahrbuch für Kinderheilkunde, Aug., 1910).

Thyroid insufficiency often underlies irregular, delayed, and erratic dentition and decayed teeth in children. Administration of thyroid is markedly effective especially in **delayed dentition** and children bordering on **cretinism**. The writer invariably starts to regulate the teeth of a young child by giving thyroid. M. C. Smith (Boston Med. and Surg. Jour., Oct. 19 and Nov. 9, 1916).

The writer found that in some cases of **hypothyroidia**, in which the administration of animal thyroid preparations only partially controlled the symptoms, they were almost completely relieved by human thyroid extracts. S. P. Beebe (N. Y. Med. Jour., civ, 445, 1916).

Hypothyroidia, in so far as nutrition is concerned, may be defined, therefore, as that condition of the body in which, owing to deficient production of the thyroparathyroid secretion, cellular metabolism is slowed sufficiently to inhibit more or less all functions. Hence, the value of thyroid preparations in **infantile marasmus**.

In **infantile wasting** the writer gives thyroid in a diluted milk and cream mixture with sodium citrate, 1 or 2 grains to the ounce of milk. In a day or two cream is gradually added, ½ a teaspoonful to the feeding bottle. Out of 80 cases thus treated 72 were infants under 9 months and their history was simply one of wasting. The other 8 had a wasting supervening on some acute diseases; 63 cases did well; 5 cases presented syphilitic histories in which wasting was a marked symptom. Mercury was first given and later thyroid. Three immediately gained and eventually recovered. In older children the results have also been favorable, except when tuberculosis was present. In children under 9 months, the author began with ⅓ grain of dried thyroid once daily. Larger doses often seemed to induce a diarrhea. In the giving of thyroid it is advisable to test the stools frequently to see whether they are acid or alkaline. In case acidity is found the bicarbonate of soda may be given three times daily, and when the natural alkalinity of the stools is restored the thyroid will begin to exert its beneficial results. No grave symptoms followed the thyroid therapy. In 6 cases a punctiform rash appeared, confined in 2 cases to the front of the chest. It was evanescent and disappeared without treatment in the course of twelve to twenty-four hours. In only 1 case was it necessary to stop the thyroid (three days) in order to cause the rash to disappear. J. W. Simpson (Brit. Med. Jour., April 30, 1910).

Its administration to mothers who have not enough milk for their babies has, in the writer's practice, with one exception, been followed by an increase in the flow, making it possible to get along without artificial feed-

ing where such feeding had been necessary with former children and would have been necessary in these cases, as shown by decreased flow whenever the thyroid was withheld. E. W. Demaree (Western Med. Rev., May, 1910).

The symptoms of typical **hypothyroidism,** besides the adiposis, are scanty or absent menstruation, drowsiness, slow pulse, dry skin, local puffiness and perhaps slow mentality. The writer cautions against the careless use of thyroid. It should be added to the list of poisons and never sold unless with physician's prescription. It is potent for harm, and a little too much may push a wavering thyroid gland to hypothyroidism. O. T. Osborne (Jour. Amer. Med. Assoc., Nov. 2, 1912).

The writer met with a case of double pneumonia and pleural collection which was followed by the following clinical syndrome: intense abdominal pain, constipation and slight meteorism, profuse sudation, normal temperature and a slow, irregular pulse. At autopsy the writer found a hemorrhage in both suprarenals; the medullary substance was entirely destroyed in 1, and greatly involved in the other. The cortex of the glands was preserved. The writer points out the concordance between the clinical signs offered and the physiological data known, which show that the disturbances arising in this case resulted from a lack of tonus of the sympathetic, that is to say, from an adrenalin insufficiency. Löwenthal (Berl. med. Woch., Nov. 25, 1918).

In contrast with this condition, and exemplifying clearly what we are to expect from thyroid preparations, is the opposite condition—hyperthyroidia. **Hyperthyroidia, or Hyperthyroidism.**—The opinion of Möbius that exophthalmic goiter or Graves's disease is due to overactivity of the thyroid (treated in full in the fifth volume)

has steadily gained ground. But this imposes the necessity of establishing clearly the diagnosis of this disease, for there are many disorders that are due to thyroid overactivity, the so-called "larval" or "aberrant" types, the "formes frustes" of the French, or "pseudo-Graves's" disease, which should not be confounded at all with true exophthalmic goiter, since the active or erethic stage of the latter is aggravated by the use of thyroid preparations, while the "pseudoforms" are benefited by these agents. This does not, however, militate against the fact that exophthalmic goiter and all the above-mentioned subtypes are expressions of thyroid overactivity, or hyperthyroidism. In all we meet, more or less defined—in proportion with excess of thyroid secretion produced—the same group of phenomena, all of which can readily be explained by excessive tissue metabolism and its consequences.

Tests.—Loewi in 1908 found that the instillation of 1:1000 solution of adrenalin in the conjunctiva produced dilatation of the pupil with abnormal readiness when hyperthyroidia was present owing to the increased irritability of the dilator fibers of the iris due to the disease. Numerous observers have confirmed these observations.

The best adrenalin test is that of E. Goetsch (N. Y. State Jour. of Med., July, 1918) based on the fact that a patient suffering from hyperthyroidism is hypersensitive to adrenalin. A hypodermic syringe with a fine needle is used to inject 0.5 c.c. (8 minims) of the 1:1000 solution of adrenalin into the deltoid region subcutaneously. The positive reaction is characterized by an early rise of blood-pressure and pulse varying from 10 to 50 and normally proportional to the degree of thyroid intoxication present. There occur also the symptoms, such as asthenia, tremor, throbbing, vasomotor changes, apprehension and nervousness, which characterize a mild case, or an increase of previous symptoms.

Lymphocytosis indicates a pathological state due to toxic influences from the thyroid. It is a symptom that cannot be simulated, and has often proved of decisive value in distinguishing between functional or organic heart disease. Instillation of epinephrin in the eye also causes mydriasis that is prompt, marked and lasting for several hours, when the thyroid is functioning abnormally. Curschmann (Med. Klinik, Mar. 5, 1916).

During the great war, many cases of hyperthyroidism were observed among the troops, due to the intense stress, and exertion to which they were subjected.

Hyperthyroidism is seen very frequently in the military service age, the young and middle aged adults. Owing to its symptoms, it interferes with a soldier's duties; it is of great importance to diagnose this condition, and, if it exists, to what degree. This can be accomplished by means of **galvanopalpation** in which a positive diagnosis can be made when galvanohyperesthesia and a high degree of reaction of the blood-vessels is obtained. Max Kahane (Wiener klin. Woch., Feb. 11, 1915).

The most striking feature of cases of hyperthyroidia in the recruit in nearly every instance is tachycardia. This is the sign because of which most of the cases report to the regimental medical officer or on which they apply for exemption or discharge. It is constant in practically all examples of the syndrome, though it varies very greatly in degree. It is present alike in recruits presenting themselves for initial examination, in those who report later, and after considerable drill and army routine may have further served to upset the mental, emotional and circulatory equilibrium of these patients.

The tachycardia is rarely accompanied by arrhythmia even in cases of very marked degree, and polygraphic studies, except in instances complicated by other vascular conditions, show, aside from rapidity, few signs of abnormal action, except that in the same case there is under varying conditions usually great variation in the rate of systoles. Practically always the rate is increased by exercise, though there are exceptional cases in which, as in ordinary palpitation, exercise may slow the rate, especially when the attention is thereby distracted; but speed of action is even more constantly accelerated by excitement and disturbing emotional factors.

Closely associated with tachycardia is an obvious and subjective throbbing of the superficial vessels, notably of the carotids, of the brachials and even of the femorals, while that of the aortic, in moderately thin persons, is also quite evident. Harlow Brooks (Amer. Jour. Med. Sci., Nov., 1918).

The thyroid was found enlarged in about two-thirds of recruits examined in whom tachycardia existed, sufficiently in some to constitute true goiter and to produce pressure dyspnea. In most of these an ancestral history of goiter, particularly on the maternal side, was given. Exophthalmos was present in cases of long standing, sufficiently so, in some instances, to have produced conjunctival hyperemia and desiccation. In some, the exophthalmos had developed suddenly. Virtually all patients were rapid and large eaters, but they bore acute infections badly, while tobacco produced in them more serious symptoms than in the average smoker.

This symptom, which includes all the cardinal signs of Graves', was observed chiefly among men belonging to nationalities in which the emotional element is common: the Hebrews, Italians, and Irish, the frequency following the order named. The negroes, least of all races, showed a predilection to the disorder.

In civil life emotional stress of any kind, fright particularly in the course of accidents accompanied by traumatisms or blows, car or train dis-

asters, mental distress, worry, violent emotions, etc., are familiar causes of Graves' disease. A personal case due to an accident and rapidly proceeding to recovery under medical treatment, recurred at once after a second accident, though the patient had suffered no traumatism. C. E. de M. Sajous (Penna. Med. Jour., Jan., 1919).

Untoward Effects.—When large or excessive doses of thyroid preparations are administered, there occurs: a rise of temperature, a feeling of abnormal warmth; tachycardia due to excessive excitability of the heart muscle; pains, trembling owing to a similar condition of all muscles; sweating due to overactivity of the sweat glands; vomiting and diarrhea owing to abnormal irritability of their gastric and intestinal neuromuscular supply. Excessive metabolism involving the production of a surplus of wastes, the kidneys are overburdened and overactive, and the cutaneous emunctories likewise, the latter causing pruritus and a papular eruption, beginning, as a rule, over the scapulæ. As in Graves's disease, hyperthyroidism and excessive doses of thyroid may produce apparent protrusion of the eyeballs, the palpebral muscles being retracted owing to their abnormal contractility and changes in carbohydrate metabolism.

In a study of 27 cases of hyperthyroidism, excess of sugar in the blood was found to be a very common accompaniment of the latter condition, occurring in 90 per cent. of instances in the moderate and severe types of cases. Glycosuria, either spontaneous or alimentary (100 Gm. of glucose having been given), was an equally constant symptom. Alimentary hyperglycemia and glycosuria were even found not uncommonly in the very mild cases. Marked diagnostic significance is attached to the lowered carbohydrate tolerance in hyperthyroidism, its presence being highly suggestive where alcoholism, fever, asphyxia, neurasthenia, and the various other ductless gland disorders can be excluded. H. Rawle Geyelin (Arch. of Internal Med., Dec., 1915).

The writer describes cases in which the condition of hyperthyroidism was the cause of the carbohydrate tolerance being destroyed. His first case presented the classical symptoms of the 2 diseases, diabetes mellitus and exophthalmic goiter. Not suspecting that the glycosuria might be related to the coexisting Graves's disease, the latter was regarded as the lesser of the two evils and treatment directed entirely toward the former. A total restriction of carbohydrates was unavailing in securing sugar-free urine. While the percentage was reduced, the sugar content of the blood remained unchanged. The patient finally died in coma.

Before the second patient with the same syndrome was encountered, the author having acquired some experience with the boiling water injections of Porter, applied this method to his second case together with the usual dietary treatment of diabetes. The goiter was injected daily, about 60 minims (3.75 c.c.) of boiling water being used. In 4 days a carbohydrate tolerance was gained, increasing with each succeeding injection till, finally, with extirpation of the goiter, normal tolerance was completely restored.

Reference is made to the work of Sainton and Gastaud of Paris, and the statistics given by them show the frequency of diabetes in exophthalmic goiter as 3 in 100 cases. Clinically, diabetes occurring in the course of Graves's disease is manifest in two ways: (1) as a temporary or slight glycosuria with the usual symptoms of diabetes only present in a trifling degree, (2) as a well-established condition, with all the characteristic symptoms present, the latter frequently even dominating the clinical picture as a whole. The possibility of the adrenals participating in such

a glycosuria is considered, owing to the thyroido-adrenal origin of exophthalmic goiter as taught by the Vienna school. This teaching is based on the theory that a relation exists between the thyroid, pancreas, and chromaffin system. J. C. O'Day (Surg., Gynec. and Obstet., Feb., 1916).

A case of thyroidism in an infant from administration of thyroid extract to the mother, a woman aged 34 who had exophthalmic goiter, was observed by Bramwell. On December 24th thyroid extract (two 5-grain tabloids daily) was administered to the mother. On January 1st the child had been sweating profusely for several nights. It was looking ill and was sleepless. It had vomited every morning for three days. The extract was consequently stopped for five days. The child immediately improved, and on January 4th was quite well. On the 9th, thyroid extract was again given to the mother. The next day the child vomited, was again restless, did not look well, and sweated profusely, etc. The child was weaned and after this remained perfectly well.

The administration of thyroid gland substance, or thyroid extract, is capable, if given in sufficient amount, of inducing a toxic state which in almost every essential is similar to Graves's disease. An artificial state of **hyperthyroidism** is thereby produced, which duplicates almost in full the morbid syndrome. Even the characteristic exophthalmic symptoms have been observed after thyroid feeding by Auld, Béclère, and others, and Edmunds was able to induce proptosis, widening of the palpebral fissure, and dilatation of the pupils in six monkeys by this means, even after excision of a portion of the cervical sympathetic. A. R. Elliott (Amer. Jour. Med. Sci., Sept., 1907).

To determine the relation between the thyroid and the reproductive life of women, the writers studied 1000 cases, 550 being primiparæ and 450 multiparæ. In these 97 cases of enlarged thyroid were found, i.e., in 64 primiparæ and in 33 multiparæ. A family history of goiter was present in 8 cases (7 primiparæ, 1 multiparæ). In 6 primiparæ there was a history of menstrual disturbance. **Hyperthyroidism** was present in varying degrees in 7 cases and probably in 1 other case, although there was no palpable thyroid in this case. Of the whole series of thyroid enlargements 20 cases had already been known to have some degree of goiter before pregnancy; 30 cases developed during the pregnancy; while 47 cases were doubtful. Markoe and Wing (Bull. Lying-in Hosp. of City of N. Y., Nov., 1912).

Referring to juvenile **hyperthyroidia**, the writer states that in a period of 8 years there have been 1512 patients operated upon at the Mayo clinic for exophthalmic goiter. Of these but 5 were under 10 years of age. In each there was a firm, noticeably enlarged thyroid apparently hyperplastic to the touch. The following symptoms were noted: vasomotor disturbance of the skin in 1, tremor in 3, mental irritability in 4, tachycardia in 5, exophthalmos in 5. All the other features observed in the disease in adults participate in the vigorous activities of their associates without apparent cardiac or muscular distress, while none of them even approached the crisis so frequently seen in adults. W. H. Lewis (St. Paul Med. Jour., Feb., 1914).

The writer found signs of excessive or perverted functioning of the thyroid as the main disturbance in 66 of his first 600 patients in the Posen military hospital; in 420 others it formed part of the clinical picture. In the 66 cases of actual **thyrosis**, 11 presented gastro-intestinal symptoms as the principal disturbance and these were manifest also in 64 of the group of 420. Thus gastro-intestinal disturbance was evident in one-sixth or one-seventh of all the cases. It was mainly in the form of gastralgia, loss of appetite, eructations and sometimes a tendency to vómit. In 34 of the group of 66 there was an unmistakable tendency to goiter, and

in 254 of the group of 420 mentioned above the thyroid could be palpated. Among the total 486 men with thyroid symptoms signs of an apical process were found, probably of tuberculous origin, in 210 cases. The writer warns expressly against iodine when there is a possible tendency to thyrosis. Caro (Deut. med. Woch., Aug. 19, 1915).

Irritable heart, now so prevalent among troops, is almost invariably associated with **hyperthyroidism.** The **X-ray** is the most satisfactory method of treatment. The thyroid gland should be exposed to a full Sabouraud dose filtered through 1 or 2 mm. of aluminum each week until the desired degree of destruction and reduction in activity has been attained. Along with this treatment there should be the usual enforced **rest** and building up process. The usual period required for restoration to health is about 2 months. F. A. Stoney (Lancet, Apr. 8, 1916).

With the pathogenesis of these two syndromes clearly defined, the various disorders in which thyroid preparations are indicated suggest themselves, viz., those in which any of the signs of *hypo*thyroidism are more or less discernible. The pathogenesis of hyperthyroidism being also apprehended, the limitations of thyroid treatment also appear: the doses utilized should be adjusted in each case to the degree of hypothyroidism that is present.

The medical treatment of **hyperthyroidism,** to be successful, requires a careful study of each patient. A simple diagnosis followed by the more or less perfunctory injection of **antithyroid serum** will in a small percentage of cases be followed by favorable relief, but to restore the patient to complete good health requires a careful analysis of the conditions in each individual. The degree to which each individual patient is subjected to these measures is a matter that can be determined only by

the individual conditions in each case. 1. **Rest;** physical, mental, emotional. 2. **Diet;** rigid meat-free diet, and exclusion of all forms of stimulation, such as tea, coffee, and alcoholics. 3. Administration of **antithyroid serum.** 4. Clearing up of all chronic affections. 5. Maintenance of hygienic conditions of the intestinal tract. 6. The judicious administration of small doses of iodine, always in the form of **potassium iodide.** This agent is not indicated in all cases, and is used only when the intense activity has been controlled. 7. The proper use at the right period of the treatment of suitable doses of **X-ray.** 8. The administration of neutral **hydrobromide** of **quinine** in a small percentage of patients during the later periods of treatment.

Hyperthyroidism is not exclusively a surgical condition, although enthusiastic surgeons so classify it. The operated patient is by no means well and needs long continued medical treatment to make a complete recovery. Beebe (Interstate Med. Jour., Feb., 1918).

Cretinism.—This condition represents the extreme type of hypothyroidism in the young. The value of thyroid gland is such in this distressing disorder that it may be regarded as a specific —the only agent, in fact, which influences it at all. The earlier it is used, however, the better the results; hence, the importance of early signs of the disease, the most prominent of which are in infants (see article on "Cretinism"), enlargement of the tongue and of the thyroid, myxedematous swelling, arrest of growth, delay in learning to speak and walk, relative deficiency of intelligence, dryness and scaliness of the skin, scantiness of the eyebrows and eyelashes, puffiness of the lids, and facies of old age.

The enlargement of the tongue and of the thyroid are the most positive signs of cretinism in the infant. The

shape of the nose and the complexion are not characteristic at this early stage, and the myxedematous swellings are not observed until after the end of the first year. Early diagnosis of acquired cretinism is still more difficult. Backwardness in learning to walk and talk is the most reliable sign. In the endemic regions the parents are now being educated to watch for the early signs. Von

nitrogenous foods being more perfectly assimilated, the nitrogen excretion rises —sometimes beyond that ingested. There is loss of weight owing to absorption and excretion of the excess of fluids in the tissues—an effect accompanied by marked thirst—in some cases, as observed by Marie, and increased activity of the kidneys. The

Case of cretinism. Result of four months' treatment. Growth, 4 inches. Intellect approaching normal. (*Moore.*)

Jauregg (Wien. klin. Woch., Jan. 10, 1906).

A comparison of the metabolic activity between a cretin over 3½ years old and two normal infants 8½ months and 10 months old, showed that it was 25 per cent. lower in the cretin than in the two infants. Talbot (Amer. Jour. Dis. of Child., vol. xii, p. 145, 1916).

Soon, sometimes within a few days, the effects of whatever preparation is used begin to appear: the appetite increases, the temperature rises, and,

red corpuscles and hemoglobin are simultaneously increased.

The wrinkles and edema disappear; the harsh, dry skin becomes soft, smooth, and moist; the hair from coarse and thin becomes thick and fine. Growth is resumed, and proceeds with great rapidity in children, sometimes at the rate of one inch per month. They do not, as a rule, however, grow tall. The brain responds more slowly, but considerable intelligence is gained in most instances, at times even that of

an average child. The later in life cretinism develops, the better are the chances of improvement in this direction; occasionally none is observed. In other particulars, all degrees of cretinism, especially in sporadic cases, may be said to be improved, the best results being obtained in young children.

Series of nearly 100 cases in which three years and more have passed since treatment was commenced. All degrees of **cretinism** and all ages were unmistakably benefited by the treatment, but the best results were obtained with the younger children. Complete cure was the rule in the milder cases, without serious impairment of the hearing, when treatment was begun in early infancy (at 6 weeks in 1 case). Von Jauregg (Wien. klin. Woch., Jan. 10, 1906).

Since 1905, the Austrian government has been supplying thyroid tablets free of charge in seven endemic foci of **cretinism** with medical inspection twice a year. About 108,600 tablets were thus distributed in 1907, and 157,900 in 1908; the number of persons taking them was 1011, and 608 were still under the thyroid treatment at the close of 1908. The results are tabulated under various headings, special attention being paid to the increase in height as the most certain index of the benefit derived. Other findings are more liable to be influenced by subjective impressions. The report states that the results have been extremely satisfactory, confirming the efficacy of thyroid treatment as a prophylactic measure, especially in endemic foci of cretinism. In 677 cases followed to date marked improvement was obtained in 48.6 per cent., and only 8.6 per cent. showed no benefit from the course. The most striking proof of the beneficial influence of thyroid treatment on the growth is the fact that in 377, that is, 85.7 per cent. of all cases, the former dwarf cretin children grew to be taller than the normal standard for their age. As a rule, treatment

was restricted to school children: the oldest cretin was 26 years old. Even after 20 a number of the cretins grew much taller and the other symptoms of cretinism became attenuated. This growth at this age is so surprising that it seems as if the growing power of the preceding years had been held in reserve, until suddenly released by the thyroid treatment, when it made all its force felt in a relatively short period. A large number of the more interesting cases are cited in detail. One cretin, 20 years old, grew 11 cm., but then refused to continue treatment, as he outgrew his clothes too fast. He did not lose his milk teeth until after thyroid treatment was commenced, although those of the second dentition were in place. A. von Kutschera (Wiener klin. Woch., June 3, 1909; Jour. Amer. Med. Assoc., July 17, 1909).

Case of cretinism in a child of 4 years which looked still like a 10 months' babe. No traces of the thyroid could be discovered on palpation. Thyroid treatment was then commenced, in 3 months the child had grown 10 cm. in height, and has developed normally since, and is now lively and healthy. C. Doderlein (Norsk Mag. f. Laegevidenskaben, July, 1910).

The writer observed a case of complete **cretinism** in which normal mentality recurred in a girl 5½ years of age, who had first come under his observation when she was 3½ months old. At that time she had all the typical characteristics of cretinism. Her extremities were the shortest he had ever seen. Her head was covered with a thick mass of coarse, flaxen hair, her nose showed no development, her tongue protruded, her skin was dry, and her flesh showed no resiliency. She showed no animation, even hunger apparently forming no part of her desires. At the present time she stood 40 inches in her shoes and she weighed 43 pounds 5 weeks ago, which was more than the normal weight and height of the average child of her age. There was

apparently nothing abnormal in the condition of the child at the present time; she played and talked just as any other child. The absence of the thyroid could not be attributed to

been given twice daily. This amount was gradually increased until for a time, when she was about 4 years of age, she took 5 grains (0.3 Gm.) daily. Under this amount she de-

Thyroid extract in cretinism. Cretinic idiot, 7 years old when thyroid treatment was begun. Had ceased to develop when 3 years old. Changes after one year's treatment. Growth 6¼ inches. (*J. B. McGee:* Cleveland Medical Gazette, December, 1900.)

trauma, since there was nothing abnormal at the time of birth except that the labor was rather precipitate. **Thyroid medication** was begun at the time he first saw the child, ¼ grain (0.016 c.c.) of thyroid extract having

veloped the typical signs of excess of thyroid. For some months she had been getting 3 grains (0.2 Gm.) daily. Very soon after beginning the thyroid treatment her hair came out in great masses and her skin came off

in sheets, 2 or 3 inches coming off in 1 piece, and the child was practically made over in a few weeks. The writer thought she was worth while presenting as demonstrating the result of thyroid medication together with persistent and careful attention on the part of the mother. The case showed that if one took a case 100 per cent. cretin early and administered the amount of thyroid that nature intended the child to have, one could get a perfect recovery, provided the child had no other defect in any other ductless gland secretion. W. B. Hoag (Med. Rec., Apr. 22, 1916).

To obtain such results, however, it is important to distinguish true cretins from idiotic dwarfs in whom thyroid is less beneficial or of no benefit whatever. These are the mongol or kalmuck idiots and the micromelic or achondroplasic dwarfs.

A comparison of the metabolic activity between a **cretin** over 3½ years old and 2 normal infants 8½ and 10 months old, showed that it was 25 per cent. lower in the cretin than in the 2 infants. Talbot (Amer. Jour. Dis. of Child., vol. xii, p. 145, 1916).

In **mongoloid mixo-idiocy** the metabolism is irregular as regards the relations between the various elements of the urine (increased elimination of amino-acids). Under thyroid treatment, though, the metabolism improved, showing better oxidation by diminished elimination of amino-acids and giving normal amount of residual nitrogen and of uric acid. G. Caronia (La Pediatria, 26, 336, 1918).

Mongol or *kalmuck idiots* resemble cretins in many particulars. The mouth is kept open by the protruding and thickened tongue; the hair is dry, scarce, and coarse; the palatal arches are narrow, the development of the teeth is delayed, constipation is the rule, umbilical hernia is frequent, etc.

But their skin is less rough, and the general development is less retarded, though that of the brain, judging from the degree of idiocy, must differ but little from that of a cretin's. In this class of idiots the palpebral fissures are narrow and slope upward from the nose; the epicanthus projects markedly over the inner canthus, as is the case in most Chinese. Nystagmus, *i.e.*, oscillatory movements of the eyeballs, is also common. Thyroid treatment though much less beneficial than in cretins, is, nevertheless, productive of good. The mental torpor is somewhat improved, the constipation and hernia are counteracted, and all functions seem to be activated.

Achondroplasic dwarfs are in reality but cases of fetal rickets, are normal as to intelligence, but their face is that of the cretin, the skin, especially about the hands, also recalling that of the latter. Other physical abnormalities are abnormal shortness and deformity of the limbs, marked narrowing of the palatal arch, and delay in the closure of the fontanelles. This condition, essentially due to morbid development of the bones and cartilages, is in no way influenced favorably by the use of thyroid preparations.

The *dose* should, of course, vary with the age of the patient from ¼ grain (0.015 Gm.) by the mouth in a 1-year-old child to 3 grains (0.2 Gm.) in the adults. As tolerance varies, especially in children, small doses should be used at the start and very gradually increased until not more than 1½ grains (0.1 Gm.) of desiccated thyroid in a child and 9 grains (0.6 Gm.) in an adult are given in divided doses daily. There is no condition in which the prevailing empirical method of administering remedies should be

more rigidly guarded against than in this, since excessive doses of thyroid not only inhibit its beneficial effects by exciting violent catabolism, thus breaking down the tissues instead of building them up gradually, but they may, by doing so, cause death.

[What unfavorable results have been recorded can usually be ascribed to excessive doses. A certain critical author remarks, for instance, referring to personal experience of this sort: "There was no longitudinal growth of the bones nor any poisoning to be observed, but great bodily prostration and an augmentation of mental apathy, together with emaciation dependent upon a loss of fat. From these unfavorable results of therapy it is seen that the view is untenable that athyreosis is the cause of cretinism. These observations are the reverse of the favorable ones made on the treatment of myxedema by thyroid gland, both in the young and in adults." The great bodily prostration, emaciation, increase of apathy, etc., speak for themselves. They had been caused by the excessive doses the critic had administered. C. E. DE M. S.]

The doses in which thyroid extract is usually prescribed are many times too large. The ordinary dose is officially quoted as from 3 to 10 grains. There are very few people, except certain types of lunatics, who will tolerate such doses under any circumstances, and not even they are able to do so unless this dose is arrived at by a gradual increase from small beginnings. It is a clinical fact, well recognized by those who have any real experience in the use of the drug, that, the more the patient requires thyroid extract, the smaller should be the initial dose. Since the writer has been using it he has been driven back and back in his doses He now seldom begins with more than $\frac{1}{4}$ grain three times a day. He never prescribes a larger dose than 5 grains thrice daily, and then only in pronounced myxedema after several weeks' treatment. He has had many patients who were unable to take more than $\frac{1}{20}$ grain once a day, but this was in each case quite sufficient completely to protect them from the symptoms of which they originally complained. In connection with the allotrophic disease, he suggests that the prophylactic dose for an adult should not exceed $\frac{1}{10}$ grain three times daily, and that $\frac{1}{4}$ grain three times daily is quite a sufficient therapeutic dose to start with. Leonard Williams (Practitioner, Nov., 1911).

The writer summarizes his results in 41 cases of sporadic cretinism in respect to physical development, mental development, retardation of mental and physical development, and the age at which treatment was begun, and offers the following conclusions: (1) Under thyroid treatment, if begun early the physical development may reach normal. (2) When treatment is begun late the physical as well as the mental development may remain much below normal. (3) The improvement in the mental development is never as great as in the physical. (4) The earlier the treatment is begun the better the results as far as mental development is concerned. (5) In congenital cases, if the treatment is begun after the first year, marked intellectual retardation persists. The later the treatment is begun. the more marked will be the retardation. (6) To obtain good results the treatment must be regular and continuous. A case presented well illustrates this point. While the treatment was regular the increase in height was $3\frac{1}{2}$ inches in a year, whereas during the periods when it was irregular it was as low as $\frac{3}{4}$ inch in a year. (7) In the acquired as against the congenital form, the intellectual development is less retarded than the physical development. C. Herman (N. Y. State Jour. of Med. Aug., 1914).

The *danger signals* are those of hyperthyroidism, previously described, the principal of which are an increase of temperature beyond normal, tachycardia, digestive disturbances, dyspnea,

and tremor. When any of these phenomena appear, the dose should be reduced until the temperature becomes normal—which may be one or two degrees F. above the hypothermia usually observed in these cases. It should be remembered, however, that excessive doses may also cause hypothermia by inducing collapse. If the morbid effects continue, the use of the remedy should be stopped a few days and then resumed with a smaller dose. Should the hyperthyroidism persist notwithstanding, **Fowler's solution** in small doses soon arrests it. A common untoward effect is bending of the bones of the legs, owing to softening of the bones. The child should not be allowed to go about too much, or when bowing of the legs appears it should be placed in bed, as advised by Telford Smith.

> Case of **tetany** following an accidental overdose of thyroid extract in a girl aged 3 years who presented stigmata of cretinism.
>
> The treatment was suspended for a fortnight and the symptoms gradually disappeared. Then ¼ grain of thyroid extract was given *t. i. d.*, increased to ⅓ grain. During the week after resuming the drug the "accoucheur hand" was again noticed. The dose was again reduced, but later increased. One month later a slight recurrence of the "accoucheur hand" compelled reduction of the dose of thyroid. Subsequently, though, on continuous treatment no recurrence of the tetany has been observed. G. W. R. Skene (Med. Review; Antiseptic, May, 1911).

[In the above case the toxic dose of thyroid produced excessive catabolism and an accumulation of waste products in the blood. Hence, the tetany which is also produced when deficiency of thyroid also leads to accumulation of spasmogenic wastes because the latter are not submitted rapidly enough to hydrolysis, a process for which the thyroid secretion prepares the wastes by sensitizing them. C. E. DE M. S.]

An important feature of the thyroid treatment of cretinism is the necessity in practically all cases of continuing it to prevent recurrence. The only permanent benefit when thyroid is discontinued is the skeletal growth, though the original morbid phenomena never return with the same intensity.

> In an **idiotic child,** Payr, director of the Leipsic Surgical Clinic, implanted a part of a normal thyroid gland in the kidney. Mental regeneration is said to have immediately started and within 1 month the child was dismissed from the hospital with the implanted thyroid gland maintaining its functional capacity in the new body. Payr (Post-Graduate, June, 1912).
>
> In several **cretins** in whom cessation of thyroid feeding led rapidly to a recurrence of myxedema the writers were led to try practical autotransplantation of the thyroid into the thyroid capsule with success in all cases. There should be a minimum disturbance of the blood supply in the region in which the transplant is placed, and foreign bodies, such as suture material, should not come into contact with the transplant. The varying degree to which a homotransplant takes depends on the amount of reaction between the host and the tissue transplanted. A familial relationship and probably the early age of the animals on which operation was performed were shown to be important features of success. Hess and Strauss (Arch. of Internal Med., Apr., 1917).

Several cretins occasionally occur in the same family, from the same mother, long intervals between births indicating the permanence of the pathogenic influence in the parent. Herman H. Sanderson (Jour. of the Mich. State Med. Soc., April, 1906), for example, observed 3 cases in one family, the patients being 21, 11, and 8 years of

age, respectively. This points to the need of administering thyroid to the mother after the birth of a cretin, and during any subsequent pregnancy.

Occasionally a case is met in which instability of the gland may manifest by deficient activity at one time and abnormal activity at another.

> Case of a diminutive woman aged 33, who exhibited alternately, and at times even in conjunction, pronounced symptoms of **hypothyroidia** and **hyperthyroidia**. At night the patient passed into a condition verging on myxedema, while in the post menstrual period her condition suggested Graves's disease. Intervening between the hypothyroidia and hyperthyroidia were normal periods, the latter amounting, however, only to a few days in each month. It is ascribed to variations in the circulation through the thyroid, inducing alternate states of inertia and overactivity in its function. Léopold-Lévi (Presse méd., June 10, 1918).

Myxedema.—Thyroid preparations are no less efficacious in this disease, which typifies hypothyroidism, in the adult than in cretinism, of which, in fact, this disorder is the prototype in adults. Here, again, we obtain those striking changes which clearly indicate that the remedy replaces in the organism a constituent necessary to the vital process itself, and the least deficiency of which impairs all functions. This is further shown by the necessity of administering it continuously, year in and year out, as in cretinism, to prevent recurrence.

Under the influence of thyroid preparations the morbid symptoms disappear. The dense, swollen tissues rapidly recede, causing loss of weight; the projecting abdomen resumes its normal contour; the skin loses its roughness and dryness; the hair grows more or less abundantly; the face loses its

coarse and expressionless appearance, the wax-yellow color of the skin being replaced by a normal hue; the cyanosis of the lips, ears, and nose disappears. Even the slow and monotonous speech and mental torpor are promptly done away with, and if the case happens in an adolescent stunted by the disease growth is resumed and progresses rapidly, as in cretinism. The physiological action is precisely that defined under the preceding heading, since we again meet with a rise of temperature and all the phenomena that denote increased metabolic activity, including a marked increase in the urea excretion. Menstruation, frequently suspended, soon returns. The appetite markedly increases, and the patient experiences a feeling of well-being

> The writer reviewed the history of the first case of **myxedema** successfully treated by thyroid extract. The results obtained not only afforded definite proof that the thyroid gland produced an internal secretion, but showed that the thyroid insufficiency of myxedema in man could be made good by maintaining an adequate supply of thyroidal hormones from an external source. This patient, a woman of 46 when the treatment was begun, in 1891, lived until early in 1919, when she died at the age of 74. By the regular and continued use of thyroid extract she was enabled to live in good health for over 28 years after she had reached an advanced stage of myxedema. During this period she consumed over 9 quarts of liquid thyroid extract or its equivalent, prepared from the thyroid glands of more than 870 sheep. George R. Murray (Brit. Med. Jour., Mar. 13, 1920).

> **Myxedema** is insidious in its course; this renders an early diagnosis difficult. The importance of recognizing this disease lies in the fact that a sovereign remedy for it exists and that, unrecognized and

long overlooked, such cases suffer serious physical and mental developments. J. M. Anders (Trans. Amer. Climatol. Assoc.; N. Y. Med. Jour., Dec. 7, 1921).

The *dose* generally employed in this disease is, as a rule, too large; 1 grain (0.065 Gm.) of desiccated extract daily, gradually increased until 2 grains (0.12 Gm.) are given *t.i.d.* Even smaller doses have given favorable results.

Inasmuch as myxedematous patients are, as a rule, more susceptible to thyroid preparations than normal subjects, it is always best to begin with small doses, since the degree of activity of the patient's own thyroid, though greatly reduced, is an unknown quantity. The presence of unexpected activity is the main underlying cause of the so-called "susceptibility" often met with, a very small dose of the desiccated thyroid sufficing in such patients to raise the standard of thyroid activity to its normal level. Again, as I have shown elsewhere (see "Internal Secretions," 1st ed., p. 1139, 1907), there is a true cumulative action of the thyroid secretion (thyroiodase) when thyroid preparations are administered, and there comes a time when toxic phenomena appear, even under the influence of very small doses. The temperature is the best guide. As it is below normal in all cases, the doses should be regulated in such a manner as to raise it to normal, reducing them as 98.6° F. (37° C.) is exceeded. The quantity required—usually somewhat larger in winter than in summer—by each patient may thus be readily determined while avoiding cumulative effects.

In some cases it is well to ascertain whether a low blood-pressure is not perpetuating the peripheral hypothermia by causing the blood to recede to the deeper great trunks. This may be done by giving strychnine simultaneously in doses of $\frac{1}{40}$ grain (0.0016 Gm.) three times daily. By stimulating the vasomotor center, it causes the vessels to contract, and thus to project the circulating arterial blood into the peripheral capillaries. Strychnine, moreover, as shown by I. N. Love, tends to prevent the untoward effects of thyroid preparations.

An important feature of the thyroid treatment of myxedema is that the patients should be kept in bed the first few weeks and not allowed to get up suddenly, to avoid sudden syncope—the cause of death in several cases on record. This precaution is especially necessary in aged and weak patients and quite as much where the improvement is rapid as in less favorable cases. As emphasized by Combe, Seymour Taylor, and others, alcohol should not be used during the treatment.

Bourneville, Lancereaux, and other clinicians have called attention to the fact that symptoms of myxedema do not appear in infants until they are weaned. This is because the mother supplies her suckling what thyroid secretion it needs to satisfy the needs of its cellular metabolism. Thyroid administered to a nursing mother is also transferred to the nursling in such a degree, in fact, that the latter may present toxic phenomena. This suggests additional caution when the remedy is used in myxedematous women during pregnancy and lactation.

Thyroid feeding was found by the writers to increase the catalase of the blood while decreasing it in the heart and probably in the fat and skeletal muscles. The increased blood-catalase may account for the increased oxidation in animals given thyroid. Burge, Kennedy, and Neill (Amer. Jour. of Physiol., June, 1917).

Contraindications.—When any adynamic cardiac disorder is present, the initial dose should be very small and very gradually increased, giving digitalis simultaneously if indicated by the cardiac trouble. When **angina pectoris** accompanies myxedema, small doses of thyroid are beneficial, especially if the patient is placed on a vegetable diet.

beneficial effects of the thyroid preparation.

The *danger signals* when thyroid is used in myxedema are, as in cretinism: tachycardia, palpitations, prostration with sweating, rapid emaciation, gastrointestinal disorders, anemia, headache, and in some cases excitement recalling hysteria. When the doses (even though small) are too large for

Fig. 1.—True myxedema. (*Hertoghe:* Bulletin de l'Académie Royale de Médecine de Belgique.)
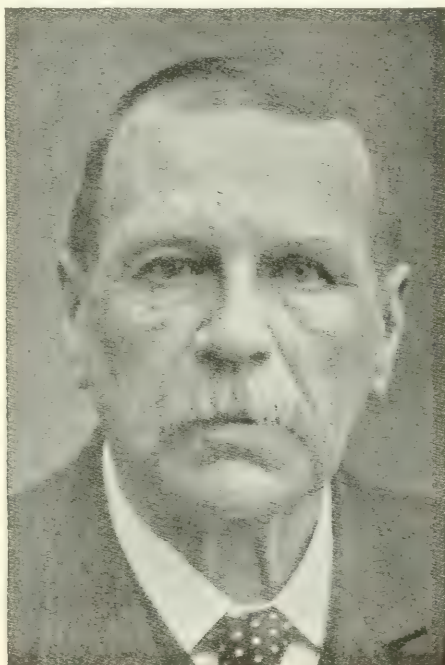
Fig. 2.—The same patient after thyroid treatment. (*Hertoghe:* Bulletin de l'Académie Royale de Médecine de Belgique.)

Occasionally aged subjects fail to respond to the thyroid treatment alone, and the disease progresses until mental aberration, melancholia, or even maniacal disorders supervene. The depressed forms of mental disorder are probably due to the low blood-pressure which characterizes the disease, and which the thyroid tends to increase. Strychnine counteracts this untoward action, however, while enhancing the

the patient, urticaria may appear. This is due to cutaneous irritation caused by the more or less toxic wastes produced in excess owing to the excessive catabolism induced, and which the kidneys cannot eliminate with sufficient rapidity. Cessation of the drug for a few days usually causes all these morbid effects to disappear, after which the remedy may be resumed in very small doses.

After recovery, the patient's health can usually be maintained, *i.e.,* recurrence of the disease prevented, by administering small doses, 1 grain (0.065 Gm.) daily or every other day—just enough to sustain the temperature up to normal. In winter it is sometimes necessary to increase the dose somewhat to obtain this result. The prolonged

Fig. 3.—True myxedema; sister of patient in Figs. 1 and 2. *(Hertoghe; Bulletin de l'Académie Royale de Médecine de Belgique.)*

use of the remedy does not, with rare exceptions, diminish the need of it to ward off the disease; cessation after several year's use will be followed by prompt recurrence of the morbid phenomena.

> Case in a man of 36 years in which, after recovery from the initial treatment by the thyroid extract (which lasted two months in continuous dosage), the patient was never under treatment longer than four weeks at one time. The longest respite from thyroid therapy was for a period ex-

tending from May, 1907, to October of the same year, a period of five months; at the end of this time some of the old symptoms were again in evidence, namely, characteristic color, loss of expression, swelling and puffiness under the eyes; the mentality, however, continued good. The patient himself wanted to be placed under treatment again. An interesting feature of the case, aside from its rarity in these parts, is that if the patient takes more than three tablets a day, now that a cure is established, or continues the treatment for more than three weeks, he soon shows the symptoms of exophthalmic goiter, namely, nervousness, sleeplessness, slight exophthalmos, nausea, sometimes vomiting and general weakness. S. E. Simmons (Jour. Amer. Med. Assoc., May 15, 1909).

Occasionally a case is met with in which the thyroid treatment is followed by permanent recovery. Such cases are probably instances of temporary myxedema due to obstruction of the lymphatics through which the secretion gains access to the general circulation, or to some other factor interfering temporarily with the functions of the gland.

Between the cases in which continuous after-treatment is required and those that proceed to recovery are some in which respites of several weeks in the after-treatment are required to obtain the best results. This is a result obtained, however, only when large doses of thyroid are used in the after-treatment. There is danger in such cases of causing hyperthyroidism, *i.e.,* the symptoms of exophthalmic goiter, and it is preferable to reduce the dose until the exact quantity required continuously to keep the patient well is ascertained.

Thyroid grafting has been performed successfully in animals, especially by

Christiani, and more recently in human subjects suffering from **myxedema or cretinism.** In the earlier operations, the improvement lasted only as long as the secretion that happened to be in the implanted tissues lasted, but in recent years better results have been obtained, the grafted fragments of thyroid assuming physiological functions to a sufficient degree to prevent recurrence of the disease.

> Case of a young woman who, becoming tired of the preventive treatment by thyroid, requested a substitute. The writers inserted portions of a sheep's thyroid gland in a series of grafts under her skin on two occasions three and a half months apart. The thyroid feeding was gradually diminished until it was reduced to a few drops a day of a liquid extract. About six months after the second transplantation the patient was delivered at term of a well-developed healthy infant. It was observed that during the latter months of her pregnancy the grafts became enlarged, evidently from congestion, being affected like the normal thyroid by the pregnancy. The successful termination of the pregnancy was ascribed in great part to the thyroid treatment, and especially the implantation of the functionally active thyroid under the skin. Lannelongue, in a case of a myxedematous infant, had previously implanted the first fragment of a sheep's thyroid in the human subject. The child's condition appeared improved, and the development of the disease became a little less active. Charrin and Christiani (Le Bull. médicale, July 11, 1906).

The best results can certainly be obtained with repeated implantation of small scraps, and for this it is better to implant the scraps in the subcutaneous tissue (Christiani) or in the peritoneal tissue (von Eiselsberg).

> Series of personal experiments in thyroid implantation showed that thyroid tissue of the guinea-pig transplanted in the same animal heals most easily and best when the transplantation is made into the subcutaneous connective tissue; likewise, the peritoneal cavity shows itself a very favorable implantation site; that transplantations into the spleen heal fairly well, but the end results are less good and not so certain as those obtained when one uses as implantation sites the two places above named; the liver and the bone-marrow are very unfavorable organs for the healing in the thyroid tissue; that thyroid transplantation promises in general more fruitful results if one avoids all bleeding in the pocket destined to receive the graft; that if one transplants the thyroid tissue in conjunction with the connective-tissue capsule pertaining to it, it is to be observed that the follicles in the vicinity of this capsule are better preserved and more numerous than the more remote follicles; that the best results are attained if one transplants into the subcutaneous tissue very thin slices of thyroid tissue instead of larger pieces; one condition is that one of the surfaces of the implanted piece is covered by the connective-tissue capsule of the thyroid. Carraro (Deut. Zeit. f. Chir., Feb., 1909).

The more recent work of Payr (1912) and of Hess and Strauss (1917) has been reviewed under the preceding heading.

Obesity.—The treatment of this condition by means of thyroid preparations was far more in vogue a few years ago than at present, owing mainly to its indiscriminate use by laymen, and to the use of excessive doses by the profession. Both these features were the cause of dangerous phenomena (and sometimes death) during the course of treatment, or of pernicious after-affects. When thyroid preparations are used intelligently, however, adjusting the dose to the needs of each

case, and regulating judiciously the concomitant diet—which in some cases means an increase—a great deal of good may be done in the great majority of cases, besides improving the appearance of the patient and his general well-being. (See article on OBESITY, in the seventh volume.)

The cases in which thyroid preparations act favorably are those in which metabolic activity, especially its catabolic phase, is deficient. The fat, ruddy boy or the plethoric, vigorous, red-faced high-liver do not belong to this category. Those that do are pale, flabby, anemic, in most instances females between 25 and 45 in which the heart beat is weak, sometimes irregular and rapid with compressible pulse. The fat in such is more or less irregularly distributed in the subcutaneous tissues; they suffer from dyspnea, especially on exertion, and fall asleep readily at any time. Such cases are in reality instances of mild myxedema in which the thyroid does not supply quite enough secretion to satisfy the needs of the organism. It is not a question of overeating with them; such patients, in fact, are, as a rule, abstemious, the slowness of their tissue exchanges causing them to have but little appetite. Unable to burn up their carbohydrates, sugars, starches, and fats as fast as they are ingested, fat steadily accumulates in all tissues.

Thyroid preparations, when judiciously used under such circumstances, are of value mainly because the rôle of thyroid secretion they replace is precisely—from my viewpoint—to enhance the catabolic phase of metabolism, essentially the function at fault in obesity. The fat-cell is rendered more susceptible to oxidation—along with the other tissues—and the excess of fat is steadily consumed.

Series of about 100 cases of **obesity** in which thyroid extract was used. No untoward symptoms were noticed in any of the cases, malaise, headache, palpitation, and nervous derangement being entirely absent. Albuminuria was not seen at any time. The thyroid gland used in all instances was B. W. & Co. tabloids. The initial dose was 2½ grains with each meal, either mixed with the food or taken with a little water. After seven days the dose was increased to 5 grains with each meal, and this dose was not increased in any case. The tabloids were crushed before being taken. In the successful cases summarized below no alteration in diet was ordered, the patient eating and drinking anything he or she desired. Alcohol was, however, strictly prohibited in any form.

Of 78 females treated 69 were between 25 and 45; their average weekly loss was 2½ to 4 pounds, and the result was permanent cure; 9 were between 15 and 19, and there was no permanent result in any of them. Of 25 men 9 were between 30 and 47; they lost on an average 2 to 3½ pounds weekly; the cure was permanent; 11 men between 30 and 47 lost 1 to 1½ pounds on an average, but the result was not permanent; on 5, between 14 and 17, there was no effect at all. W. J. Hoyten (Brit. Med. Jour., July 28, 1906).

The writer emphasizes the necessity for distinguishing between obesity due to overeating or laziness and **obesity** for which some constitutional cause is responsible, as treatment varies widely with the factors involved. In the exogenous type, overeating and lack of exercise may combine to induce the obesity; the tendency to overeat and to refrain from exercise may be due to abnormal instincts, possibly the result of reflexes perverted from normal by some chemical influence. It is usually possible in time to train these

instincts into normal routes. Reasoning, compulsion and psychic measures are usually necessary, in addition to diet and exercise, in these cases. The other type of obesity, the endogenous, constitutional type, he regards as traceable to abnormal thyroid functioning. Congenital or acquired weakness or degeneration of the thyroid may induce the obesity directly or the thyroid may become a factor in the obesity only secondarily, as in case of pancreas disease (demonstrated only experimentally as yet); disease in the ovaries or testicles (deficiency of the interstitial substance); disease in the pituitary body (adiposo-genital dystrophy); disease in the pineal gland or thymus (both dubious). There may also be a combination of both the exogenous and endogenous type, especially in the young.

Throughout the endogenous forms, abnormal thyroid functioning is common to all, and treatment of constitutional obesity must be based on **thyroid treatment**. It is unquestionable now that the reliance on thyroid treatment is increasing, the dread of it diminishing.

The dangers from thyroid treatment are just as great as ever, but we know better how to watch out for them and guard against them.

The writer adds that even in cases amenable to systematic dietetic measures alone, the prolonged restriction of the diet seems to him more of an evil than a course of thyroid treatment.

With this the diet need not be so strictly regulated and the effect of the thyroid treatment is often permanent, so that the patients can eat like other people afterward without bringing back the obesity.

During the thyroid course ample provision of albumin should be ensured. The urine should be examined often for sugar.

The tendency to acceleration of the heart action and reduction in blood-pressure can be warded off by daily small doses of some digitalis preparation.

Thyroid treatment is not required in the exogenous type of obesity, diet and exercise answer the purpose, and without training in this line the obesity will return whether thyroid treatment has been taken or not. Apparatus to reduce obesity by electric contractions in the muscles are ridiculed by the writer as unable to induce any appreciable effect on the oxidation processes beyond the effect of suggestion. In conclusion he urges physicians to keep up a constant warfare against the "patent medicines" advertised to cure various ills, and especially the obesity cures, as they are by no means harmless remedies. Von Noorden (Jour. Amer. Med. Assoc.; Therap. Monats., Jan., 1915).

The writers observed the case of a woman who had been thin until the age of 18, when she contracted syphilis; she then began to increase in weight, finally reaching 157 kg. (345 lbs.), although only 1.6 meters (5 ft. 3 in.) tall.

The pituitary was found normal, but both thyroid and ovaries were pathologic.

There were 7,756,200 erythrocytes to 11,320 leucocytes, with Arneth displacement to the left.

There was very little fat around the heart, but the myocardium showed degeneration, and this was probably responsible for the sudden death.

The histologic findings in the thymus showed functional persistence. Marañon and Bonilla (Revue Neurol., Sept., 1920).

Contraindications to the use of thyroid preparations in obesity have been elaborated by various observers; but perusal of their work indicates clearly that they have been administering excessive doses. Such doses are always dangerous in the obese, since the heart is itself invariably fatty, while, conversely, small doses are always helpful because they very gradually rid

the heart of the fat which compromises its functions and eventually causes death when the patient has not been carried off by some intercurrent disorder. Even moderate doses have not proven harmful when the patient was under medical surveillance.

The *dose* of desiccated thyroid need not exceed 1 grain (0.65 Gm.) three times daily in any case. This suffices to cause a decrease of weight of from one to three pounds a week, and sometimes more, Anders ("Practice," 8th ed., p. 1276) having observed in 2 cases under this dose "a progressive loss of weight at the rate of 4 to 6 pounds per week, respectively, without injury to the general health." Such doses do not impose upon the patient the need of modifying his usual mode of living, and his diet need not, unless excessive, be altered. When the obesity is accompanied by weakness, the appetite is usually increased, especially when, as is my custom, gr. $\frac{1}{50}$ (0.0012 Gm.) of strychnine is given with each dose of desiccated thyroid. The patient does best under these conditions when lean meats, plainly broiled, roasted, or stewed, constitute the increase of his dietary. This treatment is valuable in another direction: it tends to counteract any tendency to constipation that may be present.

Danger signals or *untoward effects* are not met with when small doses are given, as previously stated, but the physician has occasionally to treat some victim of excessive dosage.

A case was observed by Notthaft in which a man took for **obesity** nearly 1000 5-grain tablets of thyroid extract within five weeks. After the first three weeks he began rapidly to develop the symptoms of acute

Graves's disease. When thyroid was stopped and the patient was put upon arsenic all the symptoms disappeared quickly, excepting the eye changes and the goiter, which were still notable for about six months.

The untoward effects most frequently met with in obese subjects are of cardiac origin: marked discomfort in the precordia, dyspnea with tendency to heart-failure. In some instances this has been followed by death when marked fatty degeneration happened to be present. But, as stated, these do not occur when small doses—1 grain (0.065 Gm.) of the desiccated thyroid—are used. Even the greatest watchfulness will not prevent toxic effects when large doses are administered, since the accumulation of the thyroid principle proceeds at a rapid rate and the milder symptoms of thyroidism are almost at once followed by its acute manifestations—those previously described.

Miscellaneous Disorders.—In the foregoing diseases thyroid treatment may be regarded as a specific, none other affording satisfactory results. Its use is being extolled in many other disorders; but it is still a question whether it procures better effects or even as good results as other available remedies. These will be considered in their alphabetical order.

Acromegaly.—The reports of cases of this disease treated with thyroid have been insufficient to warrant a conclusion, the results having been contradictory. This is probably due to their empirical use. According to my interpretation of the disease: hypertrophy of the pituitary causes excessive activity of the adrenals and thyroid (which the pituitary governs) for a time, *i.e.*, during the *sthenic* period of the disease,

Given during this period, thyroid preparations can only, therefore, add fuel to the fire and do harm. There comes a time, however, usually after several years, when the enlargement of the pituitary ceases and degeneration of this organ occurs, initiating the *asthenic* period.

The adrenals and thyroid then usually reduce their functional activity inordinately, and oxidation and metabolism are inadequate for the perpetuation of the vital functions. Here thyroid (preferably with adrenal) is useful and may serve greatly to prolong life.

Instances of benefit in advanced cases have been published by various authors. Thus, Sears observed a case treated with dried thyroid gland in gradually increasing doses until 12 grains a day were taken, besides galvanism and tonics. Three months later she was feeling very much better, her memory had improved, and she spoke and moved more rapidly. She had lost over 20 pounds in weight, but felt stronger. The history of the case and the marked physical changes leave little doubt that it was a case of acromegaly, but certain anomalous symptoms—such as the puffy conditions of the eyelids, which may, however, have been simply the result of anemia, though its appearance was somewhat different; the slow speech, and the altered mental state—suggested that her condition was also associated with a loss of function of the thyroid gland.

Rolleston also refers to a woman 26 years old who had suffered from acromegaly for upward of two years, and who for a period of five months had been treated with mixed pituitary and thyroid extracts, with great improvement. At the present writing (1921),

however, the whole subject is being considered from another viewpoint which is reviewed at length in the article on Acromegaly in the present volume.

Arteriosclerosis.—As is well known, the iodides are used with benefit in this condition. It naturally follows that thyroid preparations, which owe their therapeutic activity to the iodine in organic combination they contain, should likewise prove beneficial. This

Case illustrating the association of acromegaly and goiter. (*G. R. Murray.*)

proved true in cases reported by Lancereaux (La Semaine méd., Jan. 4, 1899), James Barr (Brit. Med. Jour., Jan. 20, 1906), and other authorities. The favorable action of thyroid in these cases, however, necessitates the use of large doses—5 grains (0.3 Gm.) three times a day—enough to cause general vasodilation. As such doses are unsafe in aged subjects, who constitute the greatest proportion of our cases, its use should be limited to middle-aged patients, therefore, reserving the iodides for the former. Sir James Barr, in fact, prefers iodine to thyroid.

Arthritis, Chronic Rheumatoid.— In this disease good results are occa-

sionally obtained when no other agent will produce the least effect. Léopold-Lévi and de Rothschild, for example, describe the phenomena observed in 2 cases of chronic rheumatism with hydrarthrosis in which thyroid extract proved of distinct value. In 1 of these the hydrarthrosis followed a fall from a bicycle, and was the precursor of attacks of muscular rheumatism, all the joints being gradually involved in the morbid process. Notwithstanding seasons at Aix-les-Bains, Dax, and other stations, the patient became quite impotent, having even to be fed. The usual remedies proved unavailing, though aspirin and iodine seemed, at least for a while, to be of some benefit. The patient's condition becoming steadily worse, thyroid extract was tried, beginning with $1\frac{1}{2}$ grains every other day during ten days, followed, after five days, by resumption of the remedy; then giving again only $1\frac{1}{2}$ grains every other day. This dose was gradually increased until, eleven months later, the patient was taking $7\frac{1}{2}$ grains, in divided doses, daily. Good results have also been recorded by Revilliod, Lancereaux, and others.

The beneficial effects of the drug become self-evident when its action and the pathogenesis of chronic rheumatism are interpreted from my standpoint. Briefly, while I have ascribed this disease to "inadequate catabolism of tissue wastes, and excitation, by the toxic products formed, of the vasomotor center" thyroid extract, as stated in the foregoing pages, enhances general oxidation and the destruction of wastes, by increasing the blood's asset in opsonin and autoantitoxin.

Thus, increase of appetite was the first effect noted in the cases referred to above; this is a normal result, since the greater cellular activity and catabolism created a greater demand for foodstuffs. Increased heat production soon replaced the marked and constant chilliness from which the patient suffered—an effect due to the marked increase of oxidation the thyroid extract engendered throughout the body. The dose was increased to $1\frac{1}{2}$ grains one day, then to 3 grains the next, this being continued ten days. After a period of rest of five days, 3 grains were again given daily. The pain became less—a fact due to decrease of the vascular tension, owing to increased destruction of the toxic wastes which, as I have pointed out elsewhere, excite the vasomotor center, thus causing constriction of all arteries. The sensory nerve-terminals being relieved of the hyperemia which caused the pain, the latter became less marked in proportion. Closely connected with this beneficial action was the effect on the joints, viz.: the *hydrarthrosis became reduced*. Being also due to excessive vascular tension, it is plain that by causing vasodilation, in the manner just explained, thyroid extract caused the excess of fluid to leave the joints. The dose being still further increased until $7\frac{1}{2}$ grains were taken daily, *emaciation* occurred—a well-known effect due to excessive catabolism provoked by large doses of thyroid extract.

Eleven months' treatment brought Léopold-Lévi and de Rothschild's case back to a condition of comfort, the joints having resumed their shape and flexibility—with the exception of one knee, which remained ankylosed—owing doubtless to fibrosis, a condition beyond the reach of the remedy. This does not militate against its use, however; it simply shows that the treatment was resorted to too late to avoid

irremediable organic lesions. The authors, in fact, refer to a case treated by Parhon and Papinian (Presse méd., No. 1, p. 3, 1905) in which thyroid extract had produced, though the disease was of twenty-four years' standing, "a true regeneration." When 7½ grains (in five divided doses) daily had been given some time, palpitations, tachycardia, and arrhythmia appeared. On withdrawing the remedy these untoward effects ceased, but recurred as soon as its use was resumed. This affords additional evidence in support of a fact I have often emphasized, viz.: that the beneficial effects of thyroid extract are obtained only when small doses are used.

Case of rheumatoid arthritis in which the writer was struck by the patient's rough, dry, harsh skin, crisp hair, husky voice, and deep suprasternal notch; the prominence of the trachea, and apparent absence of thyroid gland, analogy to other conditions suggesting deficiency of thyroid secretion.

Accordingly, the extract of thyroid was administered in doses of 5 grains three times daily, together with adjuvant treatment to be mentioned presently. In a month the results were remarkable. The patient could struggle on crutches from one room to another, his appetite returned, and pain was almost gone. In three months he could walk with two sticks, and in eighteen months he was able to walk three miles with the aid of one stick. His elbows and shoulders have regained their mobility almost entirely, and he has been for a year able to do without his thyroid extract without a relapse. At the present date he is able to get about well, with slight flexion of one knee and some metacarpophalangeal deformity, but is fat and well.

Two additional cases in which marked improvement occurred. In the writer's opinion the group of cases likely to receive benefit are those in which changes are chiefly confined to the synovial membranes, without erosion of cartilage or eburnation of bone, such cases in fact as Schüller describes as "chronic villous arthritis." Wilson (Brit. Med. Jour., Dec. 10, 1910).

After prolonged observation the author is inclined to believe that very few cases of long-standing arthritis exist without some degree of thyroid failure. There can be little doubt that rheumatoid arthritis (including both osteoarthritis and chronic infectious arthritis) is the result of chronic toxemia following an original acute condition in the majority of instances. In the early stages some or all of the following symptoms may occur: Changes in skin pigmentation; patches varying from a lemon color to brown; spots like bruises occurring spontaneously; occasionally white spots; vasomotor disturbances; perspiring hands and feet, or paroxysmal perspirations of other restricted areas; rashes; local anemias or asphyxia; shooting pains; muscular cramps; paresthesias; neuralgic headaches; gradually increasing flatfoot; muscular weakness; morning stiffness, etc. These symptoms may precede any noticeable arthritis. The poisons that are affecting the system as a whole may damage the thyroid, and, although at first there may be excessive secretion of this gland, sooner or later more or less failure occurs, and then is the time to begin giving thyroid extract.

Care should be taken to distinguish between thyroid failure and failure of the pituitary body. The former is associated with a slow pulse, the latter with a frequent pulse. In either case the patient may be puffy and lethargic. In simple obesity, on the other hand, patients are often bright mentally and active physically.

As to the diet in rheumatoid arthritis, meat, speaking generally, should be eaten; but if the thyroid function is imperfect, meat becomes dangerous unless sparingly taken.

It is best to give a small dose of thyroid at first. For some patients the author prescribes as little as 1½ grains (0.1 Gm.) once daily. They lack resisting power and cannot withstand the toxic effects of excessive doses. As a precaution it is well to allow a few days' interval from time to time in any case. The pulse should be watched, and if blood-pressure records are not obtainable any undue fall should be noted by the trained finger.

Thyroid treatment in chronic arthritis is, of course, merely an adjunct, and cannot be depended upon alone to deal successfully with the disease. Septic foci should be looked for and dealt with, and the author believes that in these cases all teeth should be removed, since few are healthy.

Teeth may be responsible for much gastrointestinal catarrh even when there is no actual pyorrhea.

In cases where thyroid failure has become thoroughly established, it is necessary for the patient to take thyroid in suitable doses for the rest of his life, W. J. Midelton (Pract., Jan., 1912).

The writer observed the case of a girl of 15 who had suffered 3 severe attacks of acute articular rheumatism, the last of which left a contracture of the tendons of both hands, rendering them useless. Various anti-rheumatic remedies and physical measures having proved ineffective 10 days, thyroid therapy, with no associate treatment whatever was substituted. After 6 days of treatment the benefit was apparent and at the end of 3 weeks the normal conditions of the hands had been fully restored. R. G. Pizarro (Sem. médica, xxiii, 445, 1916).

The writer has cured a number of cases with thyroid alone, where signs of hypothyroidism and dermographia were present. Léopold-Levi has emphasized the importance of ascertaining the presence of hypothyroid stigmata. Blind (Paris Méd., June 18, 1921).

When the salicylates fail in rheumatism, the concomitant administration of thyroid in small doses will cause the former to act.

Cancer.—Thyroid preparations have been tried by a number of clinicians in this disease. Some have obtained favorable results; others observed only temporary benefit; others again have observed no effect whatever. There are many indications, however, that, in due time, will prove thyroid to be a valuable agent in this condition.

Report of several cases treated by the writer with no other agent than thyroid in which recovery has persisted over 9 years, the cases treated including such forms as mammary and uterine cancer. Robert Bell (Trans. Brit. Gynec. Soc., vol. v, 1896).

In mammary cancer the use of thyroid alone was sufficient to cause the entire disappearance of the growth. In this case the writers began the treatment by giving a daily dose of 3 grains (0.2 Gm.) and increasing the dosage until the patient was taking 15 grains (1 Gm.) a day. At the time of this reporting, 2 years thereafter the patient was in perfect health and no trace of the cancerous growth could be found. Page and Bishop (Lancet, May 28, 1898).

Thyroid gave better results in the treatment of cancer than any other agent. Dennis (Jour. Amer. Med. Assoc., Oct. 19, 1901).

In a very severe case of cancer—the diagnosis and prognosis being confirmed by Sir Francis Laking—in which the termination was fast approaching and the pain and suffering were intense, the writer obtained results bordering on the supernatural. Convalescence began immediately, so that by the end of January—thyroid extract, 5 grains (0.3 Gm.) quickly increased to 20 grains (1.3 Gm.) daily, having been begun at the end of November—the patient was up and free from pain. In the following

October—nearly a year afterward— she "was quite well and was following an active life." H. A. Beaver (Brit. Med. Jour., Feb. 1, 1902).

The writer tried experimentally during the past 25 years many drugs and many gland extracts, including all vaunted agents from mixed toxins to the last recommended gland extract, and with the exception of thyroid extract, and possibly arsenic, he has never seen any definite benefit from their use. A. R. Robinson (N. Y. Med. Jour., Dec. 29, 1906).

Report of a case of multiple carcinoma of the skin and subcutaneous tissue, in a widow aged 61. The original growth had been removed a year previously, but others since appeared, and the patient's health was suffering severely. Thyroid was tried, starting with 5 grains, gradually increased to 15 grains daily. The patient quickly showed improvement; palpitation, sickness, and emaciation gradually disappeared along with the growths themselves. In less than three months they had entirely gone. The patient was practically well and had recovered her lost weight of 3 stone. This occurred in 1901. Ten years later, the patient was still well. E. Hughes Jones (Brit. Med. Jour., Feb. 25, 1911).

The causes which led many clinicians to shun thyroid were, first, too large dosage, and, second, unreliability as regards physiological action of the then prevailing preparations. Internists are found prescribing a daily dose of 3 to 6 grains (0.2 to 0.4 Gm.), with beneficial and not untoward results. Buford starts with ½ to 3 grains (0.03 to 0.2 Gm.) of the desiccated thyroid every 12 hours, and gradually increases the dose, while Stern, Percy, Middleton, Léopold-Levi, Firth, Dupug, Valmorin, Variot, Minoret, Siegmund and many other observers, all are ardent advocates of the minimum dose.

While there is no doubt that the untoward effects noted by the pioneer clinicians were to a large extent due to the excessive doses employed, yet the second factor, i.e., the unreliability of the preparations, was the greatest contributing element. H. H. Redfield (Med. Summary, Aug., 1915).

Cancer is a blood disease which has resulted from persistent autotoxemia. Healthy cell metabolism is gradually replaced by cell metamorphosis, which results in these metamorphosed cells departing from physiological control, and assuming the character of fungi. These grow upon and not within the tissue, as benign tumors do. Moreover, these are able to exist and thrive only upon a vitiated soil, which in this instance is the blood. Fungi likewise are able to exist only upon a polluted soil. So long as the thyroid gland is in a healthy condition healthy cell metabolism will continue; but this can only be the outcome of this gland and every other gland being supplied by non-toxic blood. Otherwise its functional activity will be reduced, and so we invariably find that hypothyroidism is in existence. Moreover, there also coexists atrophy of this gland in cancer subjects. Robert Bell (Med. Rec., Feb. 28, 1920).

For the time being, thyroid preparations should be used only in absolutely inoperable cases, surgery having given far better results than any other method, including X-rays and thyroid preparations. In the second place, it is a mistake to attribute specific or even curative properties to thyroid preparations alone. They only assist in the curative process by facilitating proteolysis, i.e., breaking down of the growth. The detritus is such that after its use the kidneys are greatly exposed, and cases have been reported in which fatal nephritis followed the use of large doses. Such doses are, therefore, dangerous. Small doses do quite as well; but even when these are used the patient should be ordered to drink at least one quart of water daily, preferably a mineral water, to promote

flushing of the kidney and thus facilitate the elimination of toxic wastes and detritus. One or 2 grains of desiccated thyroid three times daily usually suffice, but 3 grains can be given if no rise of temperature is observed.

Case of multiple **carcinoma of the skin** and subcutaneous tissue in a widow aged 61. The original growth had been removed a year before the author saw the patient, but other growths had since appeared, and the patient's health was declining. Thyroid medication was tried, starting with 5 grains daily, gradually increasing to 10 grains, and finally to 15 grains, daily. The patient quickly showed signs of improvement; the palpitation, sickness, and emaciation gradually disappeared *pari passu* with the gradual disappearance of the growths. In less than three months the growths had entirely disappeared, the patient was practically well, and had recovered her lost weight of 3 stone. This occurred in 1901, and at present the patient is still well and has not suffered since. The writer summarizes other and similar cases from medical literature. E. Hughes Jones (Brit. Med. Jour., Feb. 25, 1911).

Case of **cancer of the larynx.** The patient was a man 51 years of age who developed malignant disease of the larynx for which total extirpation of the larynx was done. After an attack of secondary hemorrhage the patient finally began to recover on the sixteenth day after the operation and gradual healing occurred. About three months later, a mass of glands over the right carotid sheath were found to be secondarily affected, and these were removed. He kept well for eight or nine months after this operation, and then recurrence of the growth took place and a lump as large as a walnut developed on the right side of the neck. An attempt was made to remove it, but it was found at the operation that the growth involved not only the common carotid artery, but the prevertebral muscles. Complete removal could be accomplished only by exposing a healthy portion of the common carotid, ligating it, and dissecting the cancerous mass up from below and sacrificing the pneumogastric nerve, an operation that would almost certainly have been fatal, while it gave little or no prospect of eradicating the disease. The lower portion of the mass involved the thyroid gland. Accordingly, the operation was abandoned except that a small portion was removed for microscopic examination. This proved to be cancerous. A few days later, the patient was seen on consultation with Sir Charles Ball, who suggested that thyroid extract should be given and cited 2 cases of inoperable cancerous lymphatic glands in which that remedy had been tried with success. Three-grain doses of the extract were prescribed three times daily. At the end of four months' treatment, there was distinct diminution in size of the glands. The thyroid extract was continued with the result that the growth finally disappeared completely, and the patient became quite well.

There is now a series of well-authenticated cases of cancerous recurrences on lymphatic glands cured by thyroid extract. R. H. Woods (London Letter, N. Y. Med. Jour., July 22, 1911).

The other agents indicated as such as would be warranted were the same general symptoms met in other disorders. The anemia, which, with the general vasodilation and the resulting recession of blood from the surface, gives the patient the waxy pallor sometimes observed, should be met by iron, preferably Blaud's pill, and strychnine in full doses. In personal cases, by treatment based on general principles, using thyroid only when the growths seemed to take a fresh start, they have been kept in abeyance several years, six years in one case, four years in another.

The same treatment is indicated in cases after operation to prevent recur-

rence, the aim here being to enhance the functional activity of all organs, including those which govern the immunizing processes. General tonics, especially iron and strychnine, and out-of-door life are of especial value in this connection.

Cutaneous Disorders.—After a prolonged trial of thyroid preparation in many diseases of the skin, dermatologists have come to the conclusion that they were indicated in disorders due to deficient metabolism. As recently stated by Winfield, these include the erythematobulbous type, which includes **dermatitis herpetiformis,** and the psoroeczematous type, to which belong **prurigo, psoriasis,** and **chronic eczema.**

This is fully accounted for by the action of thyroid products on oxidation and metabolism I have described. This is well shown in the effects noted by Don: 1. Increased nutrition of the skin; hence its probable remedial action in ichthyotic conditions: an effect produced without any necessary abnormal perspiration. 2. Increased action of the cutaneous glands, accelerating excretion of waste products, thus keeping the surface in a supple condition. 3. Regrowth of hair, as shown in myxedema and some cases of general alopecia. 4. Increased activity of the epidermal layers, causing desquamation of unhealthy epidermis and reproduction of a new covering, as observed in ichthyosis, psoriasis, dry chronic eczema, and also in some cases of myxedema and cretinism.

> Series of consecutive cases of **eczema** in young children successfully treated by thyroid. In the first case, 14 months old, the baby had suffered from eczema of the face for nearly a year. This had been entirely resistant to the usual applications and

internal treatment, nor was hospital treatment more efficacious. Two and a half grains of a thyroid tablet were given daily. In a little more than one month the child was entirely well. His cure persisted for nearly a month, when the disease showed a tendency to recur. The second course of thyroid was followed by a permanent cure. The 4 other cases gave similar results. Eason (Scottish Med. and Surg. Jour., May, 1908).

> Two cases of **eczematous seborrhea** successfully treated with thyroid. In the first case the scalp was normal at the end of two weeks; in the second in one month. Complete cure occurred in both cases, and has persisted. Moussous (Archives de méd. des enfants, March, 1908).

> It is pretty certainly established that preparations from certain ductless glands exert a marked influence upon those **dermatoses due to faulty metabolism.** There is a certain class of skin diseases, those belonging to the erythematobullous type and those of the psoroeczematous variety, in which the preparations coming under the head of animal therapy seem to do the most good. J. M. Winfield (Interstate Med. Jour., Nov., 1909).

In **psoriasis** thyroid is harmful when the eruption is developing, but it sometimes acts with surprising efficacy in fully developed cases. The untoward effects observed by dermatologists, however, are in great part due to the fact that they use too large doses. These, as previously stated, enhance catabolism violently and increase the waste products in the blood and, therefore, the cutaneous disorder.

> The writer treated 9 cases in this way, *i.e.,* by the administration of thyroid extract alone. In 3 it removed all traces of the disease. One of the relieved cases had proven intractable to the orthodox methods of treatment, by arsenic, chrysarobin, etc. The other 2 patients presented typical pictures of an average case of

psoriasis. In 3 of the cases thus treated the lesions retrogressed markedly, but never entirely disappeared. In the remaining 2 the treatment had no appreciable effect. It was administered on the basis of its favorable influence on metabolism. J. E. Hays (Miss. Valley Med. Jour., Jan., 1918).

Sajous states that a perfect secretion of the thyroid is necessary for, 1, proper relationship of the amount of fat to the rest of the body; 2, proper nitrogenous metabolism of the body; 3, proper health and functions of the skin and its appendages, hair, nails, etc. Hence, deficient secretion is apt to produce disturbances of skin functions and to interfere with the metabolism of proteins and fats. The skin being the largest fat organ in the body, therefore bears the brunt of the manifestations occurring in deficient thyroid secretion. It must therefore be conceivable that changes in the hormone producing organs, resulting in disorders of general nutrition as above mentioned, may influence the evolution of such skin manifestations as dermatoses and **eczemas.**

In considering the treatment, it must be borne in mind that a child with deficient thyroid secretion has lessened metabolic powers; Magnus Levy, DuBois, and Talbout, who have experimented with metabolism of cretins, found it to be very much less than normal. Talbout found that the metabolism of a cretin 2½ years old was about equal to a normal child 8 months old. This means that we must give less food to these children at the beginning of treatment and increase the food with the improvement.

Fairly large doses of thyroid should be administered at first, in order to remove results which have been produced by privation of thyroid secretion. Later, smaller doses are given to maintain a normal equilibrium and prevent a recurrence. Following improvement, the dose of thyroid which at first was sufficient later becomes an overdose, according to the writer,

increasing the oxygenizing process, and the patient begins to consume his own fat. Thyroid, therefore, should only be given when definitely indicated.

If the lesions of the skin are regarded as merely a symptom rather than a disease, greater progress will be made. In every obstinate skin manifestation, a thorough physical and chemical examination of secretions and excretions is indispensable for determining the proper method of treatment.

The clinical picture of disturbances of internal secretions should always be kept in mind, for it is very important that they should always be estimated in connection with any other symptom, since upon the proper treatment of this factor usually depends success or failure. M. H. Edelman (N. Y. Medical Jour., Mar. 9, 1918).

Thyroid has been tried in **lupus** by a number of observers. Though the results were contradictory, the bulk of the evidence indicates that it is worthy of further trial. Owing to its influence on oxidation, thyroid enhances the nutrition of the skin and thus antagonizes the destructive process while promoting that of repair. As full doses have to be used during a prolonged period, the patient should be carefully watched. Thyroid has been tried in **leprosy,** but the results were not encouraging, though the remedy was pushed as far as safety would allow.

In a case of **hypertrophic rosacea** which has resisted all forms of treatment, Isadore Dyer, of New Orleans, used thyroid with, for local use, a salve containing resorcin ℈j; rose water, ʒiv; lanolin, q. s. ad ʒvj. After two months there was decided improvement, the skin being soft and normal to the touch and the color greatly improved.

The patient was discharged cured after three months of thyroid medication.

Exophthalmic Goiter or **Graves's Disease.**—The results of treatment by thyroid preparations are reviewed under the heading of GRAVES'S DISEASE, in the fifth volume, the reader is referred to that article. This applies also to GOITER, reviewed in full in the same volume.

Hemophilia.—Thyroid preparations are extremely valuable in this dyscrasia, due to a deficiency of fibrin ferment in the blood. As this body, according to my researches, is mainly composed of the adrenal product, the increased functional activity of the adrenals provoked by thyroid preparations administered increases the blood's asset. The coagulation time in hemophilia may be brought down from over ten minutes to three or four minutes in adults by 3-grain doses of the desiccated thyroid three times daily after meals. This is effective not only in the treatment of the disease, but also when operations are necessary in hemophilics. Even such operations as removal of a kidney have been resorted to with perfect safety after the coagulation time had been reduced to three minutes.

Case in which **hemophilic epistaxis** was absolutely unaffected by ordinary therapeutic agents, and the epistaxis became so persistent and exhausting that permanent blocking of the nasal fossa was necessary. Treatment by thyroid extract exerted an immediate and beneficial effect, and was followed by cure. In three days the violent and persistent epistaxis had practically stopped. In six days, about 8 grains of thyroid extract having been given daily, the purpuric eruption ceased. Scheffler (Arch. de méd. et de pharm. mil., March, 1901).

Three cases of **operations in "bleeders"** in which the administration of thyroid extract, for some days preceding operation, as advised by Sajous, was followed by remarkable results in lessening the hemorrhage at that time. Sajous holds that the thyroid extract stimulates the anterior pituitary body, which in turn excites the adrenals to greater activity, thus augmenting the proportion of fibrin ferment in the blood, and consequently its coagulating power. This explains the action in these hemophilics, and its use is recommended as a preparatory treatment whenever surgical operation is to be undertaken in such persons. W. J. Taylor (Monthly Cyclo. of Pract. Med., July, 1905).

Incontinence of Urine.—In a large number of these cases, the enuresis is due to general asthenia, and the muscular debility which attends this state carries along with it inability of the sphincters to perform their functions at all times, especially when during sleep general relaxation prevails. The influence of thyroid on general metabolism and nutrition and the resulting increase of functional power in all organs affect equally both the cystic and urethral sphincters and thus overcome the trouble. The doses should be small in order to enhance general nutrition.

Infectious Diseases.—So far thyroid preparations have not been used to any marked extent in this class of disorders, but it is probable that they will eventually prove of great value owing to the identity of the thyroid secretion as *opsonin*, pointed out by myself in 1907, as previously stated. Several investigators, including Marbé. of the Pasteur Institute, have since found that the administration of thyroid preparations to animals increased the opsonic power of the blood.

The enlargement of the thyroid,

which can be distinctly detected by palpation, and its erethism during infectious and other toxemias indicate that it fulfills active functions in the immunizing process.

[The participation of the thyroid in general immunity pointed out by myself in 1903 and since confirmed, we have seen, explains the overactivity of the thyroid in certain disorders. But, as I have repeatedly emphasized in "Internal Secretions," vol. ii, this applies only to those diseases which are capable through their toxins of exciting the thyroadrenal center, thus evoking a protective reaction on the part of the thyroid and adrenals. Various toxins and poisons are not only unable to excite this center, but can depress it. Hence the fact that in the conditions mentioned (excepting septicemia, in which Vincent is wrong in his generalization) the thyroid gives no evidence, through tumefaction and tenderness, of overactivity. C. E. DE M. S.]

So far, thyroid preparations have been used in but few diseases. In true **infectious tonsillitis,** desiccated thyroid clears the field promptly. It does so, of course, by enhancing the bactericidal and antitoxic powers of the blood and glandular secretions. The bacteria being rendered more sensitive, that is to say, more easily digestible, they readily become the prey of the phagocytes, which are extremely numerous in the tonsils.

Thyroid gland has also been employed advantageously in **septicemia** and in recurrent **erysipelas,** *i.e.,* in streptococcic infection.

Pulmonary tuberculosis, before the disease is sufficiently advanced to compromise the mechanism of respiration, that is to say, during the *first or incipient stage,* is especially vulnerable to the action of small doses of thyroid. As I urged in 1907, the tubercle bacillus, which is also patho-

genic when dead, owes its morbid action to an endotoxin rich in phosphorus; being thus prone to oxidation, while the blood's oxidizing power is enhanced simultaneously, this bacillus is promptly destroyed.

The daily administration of thyroid gland at a time corresponding to or preceding infection with **tuberculosis,** and in such doses as are well borne, causes an energetic acceleration of the metabolism of the organism and modifies favorably the action of the experimental tuberculous and pseudo-tuberculous infection in rabbits. The animals treated with thyroid gland live longer than the control animals, and in some cases life is prolonged indefinitely. Frugoni and Grixoni (Berl. klin. Woch., June 21, 1909).

As stated above, it is only in the incipient stage that, as shown by personal experience, thyroid gland is useful to check the morbid process. Later, it produces exhaustion owing to the excessive catabolism it awakens, even in very small doses.

Insanity.—The idiocy of cretinism and the wonderful improvement that thyroid preparations bring about in young cretins suggest that a direct relationship must exist between the function of the thyroid and the organ of mind, the brain. The functions I have ascribed to the thyroid to increase the vulnerability of phosphorus-laden cells, etc., to oxidation explain this beneficial action. Briefly, the thyroid preparation raises the ability of the cerebral cells to replace the sluggish metabolism and inadequate nutrition of which it has been the seat to the level of normal metabolism and nutrition. In other words, the cerebral cells, along with those of the entire organism, are caused to burn faster; the vital process being correspondingly more active, the function of the brain, as the seat of mental proc-

esses, is sooner or later in young subjects carried on with adequate vigor.

Such being the case, we can only expect benefit when increased metabolism and cell nutrition is required, i.e., in **stuporous melancholias** due to defective nutrition, depressive states in general, when organic lesions are not present. Again, in view of the property thyroid preparations possess of promoting the proteolysis or breaking down of waste products we should expect benefit in **puerperal** and **climacteric insanities.** Clinical observation has sustained this interpretation. As a rule, however, psychiatrists have used entirely too large doses; hence the untoward effects recorded.

Lactation.—Thyroid preparations have been recommended as galactagogues by Hertoghe, Chéron, and others. In some cases on record the secretion of milk was free as long as thyroid was taken and failed as soon as it was neglected. This is obviously due to its stimulating influence on general oxidation, all functions being enhanced.

Middle-ear Disorders.—Thyroid preparations have been tried in several of these disorders, sclerosis, middle-ear catarrh, ossicular sclerosis, etc., but the results, on the whole, were not encouraging. They should be tried, however, in suppurative processes associated with general adynamia, as these often persist merely because the bactericidal and antitoxic powers of the blood are deficient. Thyroid, by enhancing these protective functions, has at least proven valuable in ulcerative disorders located elsewhere, even when osseous tissue was involved, as in osteomyelitis.

Nervous Disorders. — Epilepsy.— This disease is sometimes greatly benefited by the use of thyroid preparations, but only when small doses are used. Untoward results are readily caused by excessive dosage, as shown by loss of weight. Coincidently, meat should be removed from the diet, and the patient ordered to drink copiously of water. The spasmogenic wastes are thus increasingly broken down by the thyroid; they are formed less freely owing to the abstraction of meat, and the end products of metabolism are more readily eliminated by the kidneys owing to the free use of water. I have observed excellent results through this treatment. It must not be forgotten, however, that other factors—intestinal worms, indigestible foods, scars, dentition, alcohol, lead poisoning, syphilis, nasal growths, dental interpressure, and phimoses—may produce epilepsy, and that the cause must be removed in such cases if a satisfactory result is to be obtained.

A conclusion forces itself upon us, viz., that idiopathic **epilepsy** is always associated with defective metabolic processes. The latter may originate from many sources. There is a certain class of epileptics whose seizures are in direct relationship with a disturbed function of the ductless glands and particularly the thyroid. In such cases the reason for failure of the usual treatment lies in the want of thyroid feeding. Administration of the latter will be of great benefit. Six illustrative cases. Alfred Gordon (Penna. Med. Jour., July, 1908).

Three cases of **epilepsy** in which the simplifying influence of Dr. Sajous's discoveries as to the functions of the ductless glands and other body structures is clearly shown by good results. All three being due to the retention of excrementitious substances in the blood, and the irritating action of these poisons upon the spasmogenic centers—the indications, of course, were to destroy these poisons. Drugs known to do so by increasing the antitoxic substances through the ductless glands—mer-

cury and desiccated thyroid—were administered. To assist this antitoxic process of the osmotic properties of the blood, physiological saline solution was given as beverage. On the other hand, the sources of intoxication were as much as possible eliminated by purgation and dietetic measures calculated to prevent the accumulation in the blood-stream of any toxic wastes, *i.e.*, wastes imperfectly prepared for prompt elimination by the kidneys. J. Madison Taylor (Monthly Cyclo. of Pract. Med., March, 1909).

When epilepsy is complicated by bromism this may be combated with thyroid gland. A cachet 0.1 Gm. (1½ grains) of desiccated thyroid is given every morning for three weeks, then suspended from time to time for a fortnight. Two doses, each of 1 Gm. (15 grains) of potassium bromide, are given daily at equal intervals, say at 10 A.M. and 10 P.M., apart from meals, and dissolved in half a wineglassful or less of water. The bromide is to be given regularly without suspending the treatment. J. A. Sicard (Jour. de méd. de Paris, Nov. 19, 1910).

Two cases of cretinism in twin brothers, both of whom suffered in addition, one from epileptic seizures, the other from a marked degree of ataxia. The epileptic attacks began at the age of 23 and rapidly increased in frequency until they were of almost daily occurrence; there were occasional attacks of *petit mal* besides the seizures of *grand mal*. The attacks were greatly modified by thyroid therapy, although this patient could not tolerate more than 25 grains of the extract daily. The other twin, when 14 years old, developed a staggering gait, walking like a drunken man, and suffering severe pains about the hips; the arms soon became involved so that he could hardly write. This patient began by taking 15 grains of thyroid extract a day, and the dose was increased gradually until he was taking 45 grains a day without toxic mani-

festations. All his symptoms improved, including the ataxia; he is able to walk (though with a waddling movement) and to write, earning his living by typewriting. L. S. Manson (Med. Record, Jan. 1, 1910).

A considerable number of cases of epilepsy present symptoms of endocrine disorder which stand out more or less prominently. The administration of thyroid gland was found in some instances to have true therapeutic value. H. H. Drysdale (Ohio State Med. Jour., xii, 802, 1916).

In some cases of epilepsy the administration of small doses of thyroid gland (⅛ to ¼ grain—0.008 to 0.016 Gm.—three times a day) for long periods seemed to raise the patient's physiological level with marked benefit, thus permitting them to respond more favorably to other treatment. The diet should be so modified that the organism, already toxic, should be put to as little strain as possible, especially the liver, thyroid and other defensive glands. F. X. Dercum (Jour. Amer. Med. Assoc., lxvii, 247, 1916).

In cases of combination of epilepsy and tetany one has to examine carefully, whether the cause of these diseases is an insufficiency of the thyroid and parathyroid glands. Only in this case were very good results obtained from rectal applications of fresh thyroid and parathyroid glands at the same time. In other cases, however, not due to insufficiency of the thyroid-parathyroid system no effect can be expected from this treatment. G. C. Bolten (Geneeskundige Bladen, Haarlem, xix, 301, 1917).

Eclampsia.—It is now generally recognized that this complication of the puerperal state is due to toxemia. Thyroid extract is indicated, therefore, since it enhances the destruction of toxic wastes and other poisons.

This accounts, from my viewpoint, for the fact that a number of cases have been reported in which the con-

vulsions ceased under the influence of rather large doses of thyroid gland. Nicholson obtained excellent results with 7½ grains of thyroid extract every three or four hours, with morphine as an adjunct. Baldowsky confirmed its value in 2 cases; in the first, a multipara in the seventh month of pregnancy, a convulsion occurring, 18 grains of thyroid extract were given. The fits ceased. The thyroid was continued for two days longer—10 grains daily—and the patient seemed quite recovered. A fortnight later she again developed severe eclamptic fits, sixteen seizures altogether, which were treated by thyroid extract, with narcotic remedies, and recovery followed. The other was a primipara at term who was suddenly seized with convulsions at the commencement of labor. Thyroid extract alone was given, and the attack ceased before the rupture of the membranes. The labor took place without any unusual symptom, and the puerperium was normal.

I have pointed out, however, that the action of the thyroid is greatly enhanced by the simultaneous use of hypodermoclysis. In some cases the thyroid preparation was dissolved in the saline solution injected.

Migraine.—This disorder is now generally attributed to the gouty diathesis, *i.e.,* to the accumulation in the blood of intermediate waste products of the purin or alloxuric type. Thyroid preparations, by promoting the conversion of these toxic products into bodies that are readily eliminated by the kidneys, antagonize this pathogenic process. But here, again, small doses are alone indicated; 1 or 2 grains (0.6 to 0.13 Gm.) of desiccated thyroid during meals suffice at first, the effect being kept up after a few weeks by a single grain daily. The free use of water as beverage, abstention from red meats, and out-of-door exercise are necessary accompaniments to obtain the best results.

Asthma.—A certain proportion of these cases is also, as is well known, a manifestation of the gouty diathesis. Hence, the value of thyroid preparations owing to the antitoxic action which renders them useful in migraine.

Tetanus.—As thyroid preparations promptly arrest the tetanus that occurs after removal of the thyroid, they suggest themselves not only as prophylactics, but also to assist tetanus antitoxin. The latter sometimes fails merely because the spasmogenic poisons are not sensitized or "opsonized" to its effects, as shown by a comparatively low temperature; desiccated thyroid in full doses tends to correct this condition and to increase the chances of recovery.

Osseous Disorders.—As far back as 1897 Gabriel Gauthier showed that **delayed union in fractures** was counteracted by thyroid preparations, consolidation occurring in some instances as early as the fifteenth day. Similar results have been obtained by many observers, the proportion of successful cases being about 60 per cent. Removal of the thyroid had been found by Hanan, Steinlein, and Bayon to prevent the healing of fractures in otherwise healthy animals, thus affording a sound basis for the use of thyroid preparation. Its beneficial effects are best shown in the young, its value decreasing as the patient is more advanced.

Thyroid preparations have also been used with success in **osteomalacia, rickets,** and **osteomyelitis.** All these beneficial effects are explained by the

influence of thyroid on metabolism, all functions, including the processes of repair, being enhanced. The marked influence of the thyroid over calcium metabolism shown by Parhon, Macallum, and others is another potent factor in the marked benefit noted in these disorders.

Rheumatism, Chronic Progressive. —Following the experience of Revilliod, Lancereaux has urged the value of thyroid preparations in this class of disorders many years, but, as is often the case, the scoffers of the profession have caused the valuable observations of both these distinguished clinicians to be ignored, thus perpetuating needlessly the acute sufferings of the many victims of this disease. When its pathogenesis is interpreted from my standpoint (see "Internal Secretions" Suppl., p. 1869, 1907), *i.e.,* "inadequate catabolism of tissue wastes and excitation by the toxic products formed of the vasomotor center," the favorable influence of thyroid preparations is self-evident: the toxic wastes which provoke excessive vascular tension and pain being more actively broken down, the primary cause of the disorder is removed. Souques (1908), in 2 cases of this disease, found the thyroid gland atrophied. Many cases have recently been treated successfully. Léopold-Lévi and de Rothschild, who have had the greatest experience with this class of cases, recommend—in keeping with the teachings of my own experience, and now sustained by the experience of many other clinicians — that small doses should be used.

[As Rachford observed over twenty years ago "thyroid feeding will increase the excretion of the alloxuric bodies in the urine, and will produce an acute arthritis in a patient suffering from chronic rheumatic gout." Large doses will thus prove harmful where small doses will prove beneficial. C. E. de M. S.]

Case of a man who had suffered for thirty-six years from **rheumatism** and **gout,** with decided arteriosclerosis, high-tension pulse, heart hypertrophied, and albuminuria, who under the influence of Baumann's iodothyrin, started with ½ Gm. daily —increasing ⅘ Gm.—was relieved of the pain in the limbs, polyuria and albuminuria controlled, the heart improved, tension of the pulse lessened, although it was more rapid. Lancereaux and Paulesco (Bulletin de l'Acad. de Méd., Jan. 3, 1899).

Uterine Disorders.—Various conditions of the genital apparatus, such as the onset of **puberty, pregnancy, fibroid tumor,** which cause a distinct change in the metabolism of the entire organism, frequently produce enlargement of the thyroid gland. Again, the deficiency of the normal thyroid secretion following thyroidectomy in myxedema, cretinism, etc., is often associated with atrophic changes in the genital apparatus, as shown by Fisher, of Vienna

This clearly indicates direct association between the thyroid and the genital system, and has suggested the use of thyroid preparations. The **vomiting of pregnancy** is also benefited by their use.

They have been found of value for the purpose of arresting **hemorrhage,** whether this occur in connection with **abortion,** tumors, or **uterine malpositions.** A remarkable case of **metrorrhagia** due to hemophilia successfully treated with thyroid extract was reported by Déjace. In the disorders of **menopause,** hemorrhages, flushes, irritability, migraine, etc., thyroid preparations are of undoubted value owing to their ability to promote the

destruction of waste products, which underlie these morbid phenomena.

It is very probable that the toxemia of pregnancy is largely dependent upon faulty metabolism; at least, an insufficient metabolism is an accompaniment which greatly adds to the seriousness of the condition. Failure of the thyroid gland to hypertrophy during pregnancy is probably followed by insufficient metabolism, and may result in the various forms of toxemia of pregnancy. When there is a failure of the normal hypertrophy of the thyroid gland during pregnancy and when there is a diseased thyroid, as in Graves's disease, the administration of thyroid substance, by supplying the deficiency of the normal thyroid secretion and by diuretic action, may materially improve a faulty metabolism and thus give a favorable influence upon the manifestations of the **toxemia of pregnancy.** Ward (Surg., Gynec. and Obstet., Dec., 1909).

The writer observed 6 cases of **uterine hemorrhage** in which no pelvic disease was discernible, which yielded to treatment with thyroid gland. Salzmann (Amer. Jour. Obstet., vol. lxxiv, 812, 1916).

Summary.—Thyroid preparations have been used and recommended in many other diseases, but the foregoing seem to me to represent those in which they are productive of real good. My own experience has suggested that this would prove true, particularly as to desiccated thyroid:—

1. In diseases due to slowed destruction of toxic wastes, as shown by its action in **tetany, epilepsy, eclampsia, disorders of menopause, asthma, chronic rheumatism, migraine,** and also by those due to slow oxidation of fats, as in **obesity and Dercum's disease: adiposis dolorosa.**

2. In diseases due to lowered general nutrition of all tissues, including the bones, as shown by its action in **cretinism, myxedema,** and kindred disorders—**osteomalacia, rickets, and osteomyelitis.**

3. In disorders due to lowered nutrition of the muscular elements, including the skeletal and vascular muscles, as shown by its action in **general adynamia, neurasthenia, and myasthenia.**

4. In all cases in which the processes of repair or absorption are deficient, as shown by its action in **delayed union of fractures, certain benign and malignant neoplasms, and syphilitic tissue and bone necrosis.**

5. In infectious diseases—owing to the increase of autoantitoxin, thyroiodase (opsonin), and phagocytes—as shown by its action in **tuberculosis, typhoid fever, infectious tonsillitis, certain exanthemata,** and, in general, **infections** in which **fever** is a prominent symptom.

PARATHYROID ORGANO-THERAPY.

The two internal of these four small granules were described, as previously stated, by Sandström in 1880, while the two external were discovered by Nicholas in 1893, and also in 1895 by Kohn. Though distinct from the thyroid gland, they are in close apposition to, and sometimes imbedded in, this organ, and are supplied mainly by the inferior thyroid artery. Though histologically different from the thyroid gland, they also contain a colloid substance in which iodine occurs in relatively large proportion. That they carry on some general function is shown by the fact that their removal causes tetany, while removal of the thyroid divested of its parathyroids causes myxedema, arrests growth, and impairs calcium metabo-

lism, the bones, including the teeth, becoming soft and brittle.

The functions of the parathyroids are still in doubt; some investigators claim that they have no independent function; others that they govern calcium metabolism independently of the thyroid. A third group, to which my own researches have caused me to belong, believe that they supply a secretion which combines with that of the thyroid to carry on the functions of the latter, *i.e.*, to sustain tissue and calcium metabolism besides carrying on their antitoxic functions. From my viewpoint their secretion plays the principal rôle in the formation of Wright's opsonin in conjunction with the thyroid, as shown under the preceding heading.

[The investigations of King, Biondi (Berl. klin. Woch., xxv, p. 954, 1888), Zielinska (Virchow's Archiv, cxxxvi, p. 170, 1894), Vassale and de Brazza (Arch. ital. di biologia, xxiii, p. 292, 1895) on the thyroid, and those of Welsh (Jour. of Anat. and Physiol., April, 1898), and Capobianco and Mazziato (Giorn. Int. de Scienze, Nos. 8, 9, and 10, 1899), and others on the parathyroids, have shown that the product of these organs passes into perivascular lymph-spaces. Being then transferred to the larger cervical lymphatics, they are discharged by the right and left lymphatic ducts—the thoracic duct, according to Pembrey (Hill's "Recent Advances in Physiology," p. 579)—into the subclavian veins, and by way of the superior vena cava to the heart. Here they become merged with the venous blood of the entire organism, forming a single secretion—in accord with Gley's (La Presse médicale, January 12, 1898) view—which is then inevitably carried to the heart, and thence to the lungs. As the venous blood carrying the secretion passes to these organs to be oxygenized, the secretion itself is likewise carried to the air-cells.

The purpose of this itinerary suggests itself when we recall that, as stated by Nothnagel and Rossbach (Thérapeutique, p. 261, 1889), hemoglobin can fix large quantities of iodine. It accounts also for the fact that Gley (La Semaine médicale, May 25, 1898) and Bourcet found iodine in the red corpuscles. Being a component of the albuminous hemoglobin of these cells with adrenoxidase, however, iodine should be found in all tissues. While Bourcet (cited by Morat and Doyon, Traité de physiologie, vol. i, p. 470, 1904) ascertained that such was the case, Justus (Virchow's Archiv, clxxvi, p. 1, 1904) found it in all cellular nuclei. This latter feature is important, since, as we have seen, iodine serves to increase the inflammability, as it were, of the phosphorus which all nuclei contain. C. E. DE M. S.]

THERAPEUTICS.—The actual value of parathyroid in therapeutics has not as yet been clearly determined. It has been tried with benefit in **postoperative tetany** by several clinicians. MacCallum found large quantities injected intravenously necessary. Vassale, James, and Halsted have also had favorable results. While Birch found thyroid ineffectual, parathyroid caused recovery.

> The nucleoproteid of the parathyroid relieves the symptoms of acute tetany in dogs, but the globulin has no such power. Boiling or heating the nucleoproteid solution at 80° C. for half an hour destroys its activity, and it deteriorates rapidly when kept in solution or frozen. The nucleoproteid relieves tetany by the mouth, but more effectively when given subcutaneously or intraperitoneally. Berkeley and Beebe (Jour. Med. Research, Feb., 1909).

> Three cases found in literature and 1 personal case in which the transplantation of human parathyroids was followed by recovery. Danielson (Beiträge z. klin. Chir., Bd. xxxvii, S. 998, 1910).

In **postoperative parathyroid tetany** —which is prevented by removing only, as does Kocher, the central part of the thyroid, thus leaving intact the posterior capsule, to which the para-

thyroids adhere—the spasms may be arrested by implanting human thyroids from persons who have just died of some non-infectious disease. Implanted glands do not act at once; it is only when they assume their normal functions *in situ* that recovery occurs.

Study undertaken with a view to determine the course to be pursued by the surgeon when a parathyroid gland has been accidentally removed or deprived of its blood supply, and in the hope that it might be attended with such success as to justify the attempt to transplant this glandule from man to man. The transplantations were made either into the thyroid, the spleen, or in or behind the rectus muscle of the abdomen, and were both auto- and iso- transplantations. The writer's deductions were as follows:—

1. The autotransplantation of parathyroid glandules into the thyroid gland and behind the musculus rectus abdominis has been successful in 61 per cent. of the cases in which a deficiency greater than one-half has been created.

2. In no instance has the auto-transplantation succeeded without the creation of such a deficiency.

3. Isotransplantation has been uniformly unsuccessful.

4. Parathyroid tissue transplanted in excess of what is urgently required by the organism has not lived.

5. One parathyroid autograft may suffice to maintain the animal in good health and spirits for many months and possibly for years.

6. Excised or deprived of their blood supply in the course of operation upon the human subject, parathyroid glands should, in the present state of our knowledge, be grafted, and probably into the thyroid gland.

7. Complete excision of the thyroid lobes in dogs may be well borne for a year or more. The myxedema, which usually has manifested itself within a few weeks, has not increased after the first few months. May it subsequently diminish with the hypertrophy of accessory thyroids?

8. Parathyroid tissue is essential to the life of dogs, as has been conclusively proven by the result of excision of the sole sustaining graft. W. S. Halsted (Jour. of Exper. Med., vol. xi, No. 1, 1909).

The indifference of some surgeons in respect to the importance of these parathyroids merits severe criticism. Personal case which, their advice being followed, developed very severe **tetany.** The case was saved, only after all other measures had been tried in vain, by the implantation of a thyroid with its parathyroids, obtained from a small monkey and, one month later, of 3 parathyroids and a piece of thyroid the size of a small walnut, all obtained one-half hour after death from the body of a man who had died of Bright's disease and uremia. These tissues, placed at once in normal saline solution at 32° F. (0° C.), were implanted successfully within an hour, the simian thyroid beneath the patient's sternomastoid, and the human thyroid and parathyroid beneath her left rectus abdominis, under chloroform anesthesia. W. H. Brown (Annals of Surg., March, 1911).

An emulsion of fresh parathyroids may also arrest the spasms, but obviously only as long as the injected emulsion is active. It is administered in saline solution subcutaneously. It may prove curative, as in the case cited below, but here the parathyroids were only partly removed, the recovery being eventually due to the resumption of function by the latter.

Case treated successfully by means of an emulsion of parathyroids given subcutaneously. Five fresh beef parathyroids were placed in a 1:1000 solution of bichloride of mercury and allowed to soak about ten minutes. The glands were cut, under strict asepsis, into 5 pieces under physio-

logical salt solution. These pieces were placed in a mortar and ground into a homogeneous mass, 400 c.c. of sterile salt solution being poured into the mortar. This was then filtered and given as salt transfusion into the patient's breast. The oral use of thyroid and parathyroid extract and the feeding of raw parathyroids had proved entirely useless. Only 1 parathyroid had been entirely removed, and the 3 others only partly so. Branham (Amer. Jour. Med. Sci., vol. xlviii, p. 161, 1908).

[In this case the injured parathyroids recovered and resumed their functions. The emulsion only served, therefore, to compensate for the temporary absence of secretion following the partial destruction of the three parathyroids and did not itself bring on recovery. C. E. DE M. S.]

Meat should not be given to such cases, since it increases the tetany. The diet should be limited to milk, farinaceous foods, and fruit. Exercise is harmful by promoting the formation of spasmogenic waste products. Rest in bed or in an armchair tends to reduce the frequency and violence of the spasms.

Vassale claims that the parathyroid extract relieves **eclampsia** as certainly as thyroid does myxedema, while Berkeley tried it with some degree of success in **paralysis agitans**. The latter gives 5 to 8 glands per day, minced and eaten in a bread-and-butter sandwich.

The writer has treated in consultation and in his own practice 60 cases of **paralysis agitans** with parathyroid. Of these between 60 and 65 per cent. who have given the remedy a fair trial have spoken favorably of it and have continued the treatment. More than a dozen who began three or four years ago have greatly improved and are now only uncomfortable when they are without the medicine. The writer concludes that with such a percent-

age of benefited cases as this there seems no longer any reasonable doubt of the etiological relation between the disease and the remedy. One or 2 cases in the hands of medical friends or correspondents appear to be almost cured, though of such a disease in a patient of advancing years a "cure" is always to be spoken of with reserve. Berkeley (Med. Record, Dec. 24, 1910).

Simonine also speaks of encouraging results in **Sydenham's chorea** (5 cures), but the remedy has been tried by too few observers to warrant a conclusion as to its actual value.

ADRENAL OR SUPRARENAL ORGANOTHERAPY.

Brown-Séquard showed in 1856 that death followed removal of both adrenals in from a few hours to three days after a series of general phenomena corresponding to those of Addison's disease, viz., steady decline of the blood-pressure, intense prostration, and muscular weakness. This observation was not only confirmed by many other investigators, but Oliver and Schäfer, Szymonowicz, and Cybulski showed that adrenal extract caused a marked, though ephemeral rise of the blood-pressure and increased the power of the cardiac contractions. This was attributed to a direct action on the muscular elements of the arterioles and on the cardiac muscle, all tissues innervated by the sympathetic system. On the whole the function of the adrenals was thought to contribute to the maintenance of the normal blood-pressure and to sustain the tone of the tissues thus innervated.

[Although the above is the view generally taught concerning the rôle of the adrenals, physiologists themselves have recently reached the conclusion that it is erroneous. In a summary of the whole question in the April, 1917, number of

"Endocrinology," Professor Swale Vincent concludes, for instance, that "we know nothing of the functions of the adrenal body regarded as an organ on its own account." Not only is the blood-pressure theory of Oliver and Schaefer shown to be fallacious by recent experiments, but the antitoxic theory of Abelous and Langlois in virtue of which certain toxic substances are destroyed by the adrenals likewise. "It must be confessed," writes Vincent in this connection, "that the antitoxic theory has not been substantiated."

As is well known, I have attributed entirely different functions to the adrenals since 1903. As shown below, these have been experimentally and clinically sustained. C. E. DE M. S.]

The investigations of Young and Lehmann, Austmann and Halliday, Moore and the more recent observations of Hoskins and McClure, among others, have shown, however, that it is not the function of the adrenals to maintain the blood-pressure, since the amount of their secretion poured into the adrenal veins tends to lower it. When, however, the blood-pressure is morbidly reduced, adrenal extract, adrenalin or any active principle, acting pharmacologically, will tend to raise it.

> A quick rise in the blood-pressure of dogs was followed by a rapid fall and a secondary rise when adequate doses of adrenalin were administered intravenously (0.5 to 1 c.c.—8 to 16 minims—of 1: 10,000). After studying various hypotheses to account for this, the writers conclude that the primary rise is due entirely to peripheral action, and the secondary rise apparently to a central action of the adrenalin acting through the sympathetic ganglions. This central action can be prevented by pithing of the brain or removal of the head. McGuigan and Hyatt (Jour. Pharm. and Exper. Therap., Sept., 1918).

> To determine whether the dilator action of adrenalin was confined to carnivorous animals, the writers studied its action on the following species: snapping turtle, fowl, opossum, horse, goat, cats and dogs, ferret, raccoon, rats, rabbits and monkeys. This extensive study led them to conclude that the usual vasomotor reaction in skeletal muscle was dilatation with moderate doses of adrenalin, except in the case of rodents; and because of the uniform occurrence in other mammalian orders, as well as the presence in the monkey, it was believed that these mechanisms were also present in man. Hartmann, Kilborn and Lang (Endocrinology, Apr.-June, 1918).

> Ether anesthesia has a marked influence in diminishing the pressor response to minute amounts of adrenalin injected directly into the circulation. Hemorrhage also acts to lessen or abolish the response, and to a degree directly proportional to the lowering of the blood-pressure it causes. In the exsanguinated animal an amount of adrenalin 3 or 4 times that sufficient to produce a pressure rise of 10 to 15 mm. of mercury, under normal conditions, may be entirely without effect. The response to large doses, on the other hand, is uninfluenced by ether or hemorrhage. These facts have a practical bearing not only on the employment of adrenalin to tide over collapse, but on its possible utilization in the future to raise a low, blood-pressure to the normal height and maintain it during a considerable period. The amount of adrenalin which under normal conditions will suffice to bring up the blood-pressure may have little or no effect on an etherized individual or on one who has lost blood. Rous and Wilson (Jour. of Exper. Med., Feb., 1919).

Blum and other experimenters have found that adrenal extractives cause glycosuria by enhancing carbohydrate metabolism, while Josué has shown that they provoke arteriosclerosis, an observation confirmed by many investigators.

The action of adrenal preparations is exercised upon involuntary muscles —those of the vessels, heart, intestines, and uterus, for example. But, according to the prevailing view, this action may be antagonistic; it may inhibit the action of the intestines, act as mydriatic and promote the secretory activity of the lachrymal and salivary glands.

PHYSIOLOGICAL ACTION.— Personal researches, including a large number of experimental and clinical facts found in literature led me to the conclusion in 1903 that the physiological function of the adrenal secretion was (1) to take up the oxygen of the air in the pulmonary alveoli and carry this gas to the tissues as a constituent of the oxyhemoglobin, and (2) that it was the adrenal secretion which, as far as the rôle of oxygen in these processes is concerned, sustained oxidation and metabolism.

Referring the reader to the article on "Adrenals, Diseases of," in this volume and to my work on the "Internal Secretions and the Principles of Medicine," the main factors determined by my investigations were briefly: (1) that the secretion of the adrenals has a marked affinity for oxygen, and that, owing to its passage into the inferior vena cava, it is inevitably carried to the pulmonary air-cells; (2) that once here it absorbs oxygen—thus fulfilling the rôle of a secretion deemed necessary by various physiologists (Paul Bert, Müller, Bohr, Haldane and Lorrain Smith, and others) to account for pulmonary respiration; (3) that it becomes, also in this location, the albuminous (96 per cent) constituent of hemoglobin and the red corpuscles, the identity and source of which physiologists have failed to identify, and (4) that this albuminous constituent of the hemoglobin which I have termed "adrenoxidase" owing to its source, the adrenals, and to its identity as oxidase, is distributed by the red corpuscles to all parts of the body as an oxidizing substance.

[The essential feature is whether the adrenal product can, as I have held, convert the hemoglobin of venous blood into the oxyhemoglobin of arterial blood. This has been sustained lately by Menten (Amer. Jour. of Physiol., vol. xliv, p. 176, 1917) who found that the addition of adrenalin to diluted human venous blood caused an increase in the intensity of the oxyhemoglobin absorption bands. Kariya and Tauska (Jour. Tokyo Med. Assoc., vol. xxvi, No. 20, 1913) had already noticed in a study of hemolysis, that adrenalin acted as hemoglobin when fixed from the red corpuscles. C. E. DE M. S.]

This interpretation explains the phenomena that attend the use of adrenal extracts, adrenalin, etc., in therapeutic doses. The rise of temperature noted by Morel, Lépine and the concomitant rise of temperature and increased metabolism noted by Oliver and Schäfer are due to increased oxidation. It explains also the rise of a low blood-pressure, since increased metabolic activity —excited directly by the adrenal principle besides that due to general oxidation—of the muscular coats of vessels is manifested by contraction, and, therefore, by elevation of the blood-pressure. The increased power of the heart is the obvious outcome of increased metabolism in the myocardium, precisely as it is in the vascular muscles, while the slowing of its action is due to the greater diastolic expansion that attends increased functional vigor and the greater resistance the blood-column offers as a result of the increased blood-pressure.

The same process explains the phenomena produced by adrenal extractives which appear quite discordant from its more familiar effects on the blood-pressure, the heart, etc. They produce arteriosclerosis by causing excessive contraction of the vasa vasorum, from which the arterioles receive

their blood. The walls of the arteries these minute vessels nourish being partly or completely deprived of blood, they degenerate, and sclerosis follows. Glycosuria is also the result of excessive metabolism; the pancreas, as are all other organs, being rendered overactive, its ferments are secreted in excess. Amylopsin being one of these, the hepatic glycogen is converted into sugar in quantities exceeding the needs of the tissues, and the unused sugar is eliminated by the kidneys. Increased metabolism likewise explains the abnormal activity of the lachrymal and salivary glands.

Finally, the antagonistic effects of these agents are accounted for by the fact that, while the intestinal vessels are contracted through the excessive metabolic activity produced in their muscular coats, the intestines themselves are relaxed because the volume of blood supplied to them is reduced by the undue constriction of their vessels.

[The participation of the adrenal secretion in this phenomenon is shown by the fact that the supposed inhibitory action of the sympathetic on intestinal movements (which, as I have shown in "Internal Secretions," is merely an experimental phenomenon brought about by excessive constriction of the intestinal vessels) is offset by severing the nerves to the adrenals. This fact, first observed by Jacobi (Arch. f. exper. Pathol., Bd. xxix, S. 171, 1892), proves, from my viewpoint, that two sources of vasoconstriction (manifested by elevation of the blood-pressure) must always be taken into account: (1) that due to vasomotor nerves, and (2) that due to increased activity of the adrenals. It is by producing a similar constriction of the arterioles that opium and its analgesic alkaloids cause constipation and relieve pain—according to my views. C. E. DE M. S.]

Although the contention of physiologists that the adrenals do not destroy poisons through their secretion, as believed by Abelous and Langlois is warranted, the fact remains that in the light of my views the adrenals *indirectly* and in conjunction with other substances, take part in immunizing processes. We have seen under the heading "Adrenals, Diseases of," the striking influence of adrenalin in terminal hypoadrenia. This is undoubtedly due *in part* to the influence of the adrenal principle upon general oxidation; this function taking part in all protective functions, while enhancing the formation of antigens.

The writer conducted experiments which tended to show that one of the functions of the adrenal glands was to assist by means of their internal secretion in *counteracting pathological processes or products which might tend to produce* an *abnormal constriction* of the *bronchioles*. D. E. Jackson (Jour. Pharmacol. and Exper. Therap., Sept., 1912).

Adrenalin prevents absorption of poisons, in **poisoning by** non-corrosive substances such as **cyanide, strychnine,** and **aconite,** and thus permits of the stomach being emptied or a suitable antidote administered. It should be given at once, followed by the antidote or the stomach-pump. Another small dose may be given to prevent absorption of any remaining poison. J. L. Jona (Brit. Med. Jour., Feb. 8, 1913).

Experiments including the use of violent cardiac poisons, anagyrine and nicotine, showed that after the destruction of all central vasomotor connections, effects which could only be attributed to the adrenals. We must, therefore, recognize two classes of cardiac stimulants: those which act through the nervous system and those which act through the adrenals. This he regards as a new fact in our knowledge of the rôle of the ductless glands in their relations to poisons. Gley (C.-r. de l'Académie des Sciences, June 29, 1914).

[Nothing of the above is new. I pointed out in 1903-1907 (Internal Secretions) that it was through the adrenals that digitalis and other cardiants produced their tonic effects, and not as generally taught even now, by a direct action of the drug on the heart-muscle—an absurdity. I also urge that the toxic phenomena observed by Albanese, Langlois and others should be attributed to the participation of the adrenal secretion in a general immunizing function. It is not as "antigen" that it acts, however, as believed by Halpern. C. E. DE M. S.]

Intraperitoneal injections of extracts of guinea-pig adrenals, bring about in some rabbits the formation of substances which exhibit a vasodilator property in frogs. The writer deems it justifiable to consider these substances as antibodies with *adrenalin as an antigen.* Halpern (Archiv. f. exper. Pathol. u. Pharm., Oct., 1913).

On the basis of extensive clinical experience the writer recommends that $\frac{1}{60}$ grain (0.001 Gm.) of adrenalin be administered by *hypodermoclysis* in $\frac{1}{2}$ or 1 pint (250 or 500 c.c.) of saline solution in **general infections.** Being absorbed slowly, its action is sustained. Josué (Paris Méd., Dec. 4, 1915).

Physiologists are now teaching that the adrenal products inhibit the functions of the stomach, but this effect is only observed in animals when doses which are not used in man are administered.

Extracts of suprarenal gland vigorously inhibit gastric secretion. These extracts all contain more or less adrenalin and, therefore, it is presumable that their effect is produced by intensification of the inhibitory function which is ascribed to the (gastric) sympathetic. Adrenalin is not as active a gastric inhibitor as suprarenal proteins obtained from extracts of the whole gland. These suprarenal nucleoproteins contain only traces of epinephrin. Extracts of the pituitary gland also inhibit gastric

secretion, but only about one-half as vigorously as do extracts of the suprarenal. Rogers, Ablahadian and Cornell (Amer. Jour. of Physiol., Feb. 1, 1919).

Practical experience in many cases has shown that far from inhibiting the gastrointestinal canal, adrenalin promotes, even when given a long time, its functional activity.

The soft and elastic arteries in children and the integrity of the cardiovascular and other systems render adrenalin peculiarly effectual in pediatrics. It seems to have a general tonic and an antitoxic action as well as its direct vasoconstricting effect. Except in very urgent conditions, administration by the mouth is preferable. This is harmless while it avoids abrupt changes in the circulation. Its action is more protracted by the mouth, and it seems to stimulate the centers, possibly by way of the sympathetic system. The dose is from 10 to 30 drops of the 1 to 1000 solution. A. Galvani (Rivista di Clin. Pediat., May, 1918).

The writer has obtained good results in dyspeptics with **gastric atony** by prescribing 8 to 10 drops of 1 : 1000 adrenalin solution 1 hour before each of the 2 main meals, lunch and dinner. The results consisted in a diminution or disappearance of postprandial discomfort or sensation of weight, a diminution of splashing sounds, and cessation of pain. Pron (Presse méd., June 10, 1918).

Physiology of Local Action.—The local application of an adrenal principle, adrenalin, epinephrin, etc., causes such marked contraction of the vessels that their lumina, when applied over small vessels, may become obliterated, thus arresting totally the flow of blood. The tissues become very pale, therefore, and even blanched. These effects, however, are of short duration. Mucous membranes are similarly affected;

hence, the frequent use of adrenal extractives on the nasal mucosa and the conjunctiva. The constrictive effect on the blood-vessels is due to a direct action on their muscular elements; applied to the eye, adrenal extractives also produce contraction of its muscles. Hence, the dilatation of the pupil, the wide separation of the eyelids, and apparent protrusion of the eyeball. From my viewpoint, the contraction of the vessels produced by adrenalin and the resultant blanching are due to the increased metabolic activity it awakens temporarily in the vascular and other tissues to which it is applied.

[The process does not differ from that which obtains in the blood. It is that of exaggerated oxidation in which the adrenalin, as I have pointed out, plays the part of a catalyzer. Poehl found that the adrenal active principle was endowed with catalytic properties. This enables it to activate greatly the process of oxidation without being itself rapidly consumed—its action recalling that of a ferment. Jolles showed, moreover, that the catalytic activity of a given volume of blood corresponded with the number of red corpuscles it contained. These corpuscles being the carriers of hemoglobin, which, in turn, contains the adrenal principle, as I have shown, adrenalin, when applied to the tissues, acts as if a large amount of oxyhemoglobin had been concentrated upon it. C. E. DE M. S.]

A simple intratracheal injection of a solution of adrenalin in a normally breathing rabbit was found by the writers to penetrate within a few seconds to the alveoli, chiefly those of the left lower lobe; absorption was rapid and well maintained, and the procedure could be repeated effectively a number of times. Absorption of adrenalin from the lung could also be obtained at a time when double the dose given intramuscularly exerted no blood-pressure effect whatever; it continued also after the development of pulmonary edema.

Auer and Gates (Jour. Exper. Med., June, 1916).

It has been taught that adrenalin produced an increase in blood-pressure, but if there was one thing adrenalin does not do it is that. Adrenalin produces a fall in blood-pressure generally, though not always. In the Officers' Reserve Corps at Plattsburg the speaker tested many young men in the pink of condition with adrenalin. Within half an hour practically all had a fall in blood-pressure. That corresponded with the latest physiological laboratory findings. Adrenalin does not produce constriction of all the blood-vessels, but a constriction of the blood-vessels of the abdominal cavity, and dilation of the muscles of the thigh, whereas a larger dose produces constriction of the blood-vessels of the skin covering the thigh. If the constrictors overcome the dilators, there is rise in the blood-pressure. Walter Timme (N. Y. Phys. Assoc.; N. Y. Med. Jour., Feb. 15, 1919).

PREPARATIONS AND DOSE.— The preparations most generally used are the dried adrenal gland, the *suprarenalum siccum* of the 1915 U. S. P., available in tablets or powder, the average dose of which is 4 grains (0.26 Gm.), and the active principle *epinephrin,* now generally accepted as the official name for proprietary preparations, including adrenalin.

A synthetic epinephrin has also been available, but there is no ground upon which it should be given preference over the active principle obtained from the adrenals. As shown by Shultz, Cushny, and others, all synthetic products are about one-half the strength of the natural.

The solution of epinephrin available is uniformly of 1 : 1000, the doses of which are: *By the mouth,* 10 to 30 minims (0.6 to 1.8 c.c.); *intramuscularly* or *hypodermically,* if the region

is massaged, 3 to 15 minims (0.18 to 0.9 c.c.), always in free dilution with saline solution. *Intravenously,* it should only be given drop by drop in large dilution with saline solution, the latter being used as in hypodermoclysis. The use of strong solutions of 1 : 1000 solution intravenously is always fraught with considerable danger. *Rectally* it may also be used freely diluted.

> Uterine injections are dangerous unless the solution be very weak. The vaginal portion of the uterus can be rendered anemic effectually and safely by injection of only 10 c.c. (2½ drams) of 200 c.c. (6½ ounces) of salt solution containing merely 1 c.c. (16 minims) of the 1 per thousand solution of suprarenin —there is no need to use a stronger concentration. Neu (Zentralbl. f. Gynäk., July 24, 1909).

> Two fatal cases due to the use of suprarenin injected into the cervix for operative purposes. The writer uses a very weak solution injected in considerable amount. It is not the amount of the drug or of the solution used, but the concentration of the solution, that does harm. A large amount of a weak solution can be used without danger, while a small amount of a strong solution will be fatal. Braun (Zeit. f. Gyn., July 24, 1909).

As I pointed out in 1907, it is very doubtful whether epinephrin, adrenalin, or any of the adrenal active principles are physiologically active in any but *hypoadrenic* or *weak* individuals. This I attribute to the fact that gastric secretions give the oxidase reactions (guaiac, etc.), thus showing that they can oxidize them before they reach the circulation at all, and are thus deprived of their physiological properties. In hypoadrenic subjects, however, even the oxidized product (oxyhemoglobin) is taken up from the intestinal canal and assimilated.

Adrenalin injected subcutaneously or into the peritoneum in laboratory animals has a marked toxic action and no adrenalin appears in the urine. On the other hand, 20 times this dosage and more, given by the mouth, causes no signs of toxic action, while considerable amounts of adrenalin are eliminated in the urine. The author thinks that under the influence of the digestive juice and of the mucosa the adrenalin becomes bound in some way which deprives it of its physiological and toxic properties. Falta (Wiener klin. Woch., Dec. 23, 1909).

This does not apply to the dried gland, probably because the active principle is bound up in organic combination. S. Solis-Cohen found, moreover, that, by masticating the dried gland without swallowing it, the physiological effects manifested themselves.

If for some reason or other injections are impracticable the same dose of the 1 : 1000 solution on a lump of sugar, inserted between the cheek and gums, as practised by Rolleston, or adrenalin tablets, containing $\frac{1}{60}$ gram (1 mg.), placed under the tongue, will serve the same purpose though somewhat more slowly. The active principle proper, is absorbed from the colon, especially when administered with saline solution as previously stated.

> At the suggestion of Sollmann, the writer confirmed these effects by a series of experimental investigations. The effects were often found to approach and sometimes to be parallel with those produced by rapid intravenous injection, owing, doubtless, to the very great vascularity of the region. The injected material, in fact, was found at times to pass directly into the venous circulation, as shown experimentally. The administration of adrenalin in this manner clinically could possibly be of serious

moment, such as causing a sudden rise of blood-pressure in cardiovascular disease, arteriosclerosis, etc. In conditions of circulatory collapse necessitating rapid stimulation, the injection of adrenalin into the submucosa of the nasal septum, or turbinals might be of much value. J. D. Pilcher (Jour. Amer. Med. Assoc., July 18, 1914).

Epinephrin, *i.e.,* adrenalin, is also conveniently put up as an *inhalant, ointment,* and *suppositories,* the strength being also 1 : 1000 in neutral oil, petrolatum, or oil of theobroma in the order of the preparations named, and some mild antiseptic to preserve the latter.

Contraindications.—Fridericia (Ugeskrift f. Laeger, Dec. 9, 1915) enumerates the contraindications against *subcutaneous injections* of adrenalin. He found in literature 5 deaths following injections. In 1 of these a large dose (0.6 Gm.—10 grains) had been injected *into a vein* in a much debilitated patient with infarction of the lungs, granular nephritis and arteriosclerosis. In all the others the epinephrin had been injected into the muscle of the uterine cervix while the patients were under the influence of chloroform. He has also found 2 deaths on record after subcutaneous injection of adrenalin, but these were in *infants,* only 3½ months old. A number of clinicians have reported unfavorable experiences with subcutaneous injections of adrenalin in cases of *heart or valvular defects* and nephritis with high blood-pressure. On the other hand, testimony is constantly accumulating as to the value of adrenalin in sudden heart weakness in the course of acute infectious diseases. It is harmful where signs of a valvular defect or *hypertrophy of the left heart* exclude bronchial asthma. With cardiac asthma there is no expectoration or merely reddish foamy masses. Fine moist râles may be heard with cardiac asthma while with asthma of the bronchial type there are rhonchi.

UNTOWARD EFFECTS.—In the frog toxic doses produce a temporary paresis, the muscles acquiring marked rigidity. This is ascribed by some to poisoning of the spinal cord, by others to a direct action on the muscles. In mammals large doses given subcutaneously cause excitement, tremor and vomiting, paralysis beginning at the posterior extremities, polyuria, and dyspnea, death ocurring either through respiratory failure or cardiac arrest. In the cat, however, which bears larger doses than other animals, the respiration ceases, as a rule, before the heart's action is arrested. This is due to pulmonary edema, according to some authors and to paralysis of the respiratory centers, according to others. When the poison is injected into a vein the morbid effects are preceded by a very rapid and marked rise of the blood-pressure.

Man is more susceptible to the action of adrenalin than animals. While a subcutaneous injection of 1 dram (4 c.c.) of a 1 : 1000 solution will hardly affect a rabbit, one-third of that quantity has produced untoward effects in normal as well as in tuberculous subjects (Souques and Morel), *e.g.,* vertigo, nausea, vomiting, severe pain under the sternum similar to that of angina pectoris, and a feeling of constriction about the chest, a rapid pulse, dyspnea, cold sweats, and coldness of the extremities.

In a case of pneumonia in a man of 65 years, injected subcutaneously 5 minims (0.3 c.c.) of 1 : 1000 solution adrenalin. About a minute after the drug was given, the patient became restless, dyspneic, facies blanched, eyes fixed, and complained of a constriction sensation around the body on the level with the heart. His pulse became almost imperceptible and thready. The condition resembled an attack of angina pectoris. An injection of an **oil solution** of 3

grains (0.2 Gm.) of **camphor** was immediately given, which acted with remarkable readiness in combating the attack. L. J. Friedman (Med. Summary, Aug., 1915).

[This is because he failed to dilute sufficiently the dose administered. C. E. de M. S.]

Intoxication may also follow the use of adrenalin when injected into cavities, such as the vagina, the rectum, the urethra, when the mucous membrane is abraded, lacerated, or denuded, thus rendering its absorption possible. The uterus and urethra appear to be especially sensitive.

Case of a man aged 26 weighing 190 pounds, heart and lungs normal, in whom, to arrest bleeding caused by manipulation of the urethra to render a stricture passable, 10 minims of a 1:1000 solution of suprarenal principle were injected through an Ultzman instillator. The patient immediately complained of pain in the stomach, and a condition of profound shock supervened. He complained of air-hunger, vomited, and lapsed into syncope. As the pulse became slower and finally disappeared, and death seemed imminent, $\frac{1}{30}$ grain of strychnine and $\frac{1}{100}$ grain of nitroglycerin were given hypodermically. In ten minutes the radial pulse began to return, and within an hour the patient left the office unassisted. Next day progressive dilatation of the stricture was practised without the aid of the adrenal preparation. Link (Central States Med. Monitor, Sept., 1907).

The prolonged use of adrenal preparations may induce chronic adrenalism, manifested by marked cardiac disorders, especially of the myocardium; dyspnea after slight exertion, tachycardia, high blood-pressure, polyuria, icteric staining of the conjunctiva, and marked increase in weight.

Case of a man who during one year and nine months applied daily to the conjunctiva, as a treatment for con-

junctivitis, a solution of adrenalin chloride. Palpitations, with marked increase of the arterial tension, cardiac dyspnea on exertion, and polyurea, were followed by a yellowish tinge of the conjunctiva such as that observed in jaundice. A curious feature of the case was that the patient gained in weight rapidly. Cessation of the instillations and regulation of the diet caused a gradual retrogression of these symptoms, but there remained some cardiac weakness. K. Feiler (Med. Klinik, May 17, 1908).

The writers observed 10 and 20 days after an injection in dogs, the characteristic phenomena of *anaphylaxis* on injecting another dose of $\frac{1}{65}$ grain (0.001 Gm.) of adrenalin and a weak dose of thionin, normally inactive. The usual primary rise of pressure and the secondary depression were observed. Gautrelet and Briault (Soc. de Biol., July 12, 1913).

Local applications are sometimes followed by untoward effects in the tissues to which epinephrin solutions are applied. Repeated applications, especially with the atomizer, of anything but weak solutions (1:10,000) to the nasal cavities or pharynx may give rise to edema of the nasal mucosa, the uvula, tonsils, or pillars of the fauces. This is ascribed by most writers to "violent vasomotor constriction of the blood-vessels" and the resulting "venous stagnation." In some instances they cause persistent sneezing and acute coryza accompanied at times by severe pain in the upper portion of the nasal cavities.

Case of a man aged 39, of good habits and good health, except for his periodic attacks of hay fever, who was advised by a lay friend to use one of the well-known preparations of the suprarenal gland, and supplied himself with the remedy and an atomizer in the summer of 1905. He used it several times a day during his attack.

When the hay fever subsided he noticed that there was a fullness in his nose that did not disappear, but, on the contrary, became more marked. He was treated by his physician for a time without relief, and then sought the aid of a rhinologist. The condition refused to yield to any form of treatment, and, symptoms of Eustachian congestion supervening, it became necessary to remove portions of both middle turbinates. After a long course of treatment he went to his home improved, but bearing traces of the condition with him. Two other very similar cases witnessed. B. H. Potts (Jour. Amer. Med. Assoc., Oct. 13, 1906).

Adrenalin, when applied to the gums on cotton-wool—whether to stop bleeding or, as has been recommended in the preparation of cavities, to control the saliva exuding from the mucous glands at the neck of the teeth—should be used with great caution. The cotton-wool with the adrenalin solution should be thoroughly squeezed to remove excess before applying.

The writer had occasion to witness recently a distinct case of adrenalin poisoning in which it had been used to stop bleeding. Evidently in this case the adrenalin had been applied freely, and, on pressure being used to the pad of cotton-wool, a few drops of the excess adrenalin had been squeezed out. The symptoms were alarming, being not unlike an epileptic seizure, and the patient remained in a collapsed condition for some hours after. Anonymous (Chemist and Druggist; Prescriber, March, 1911).

Some cases have been reported in which sloughing and gangrene of the mucosa occurred. Elderly subjects are prone to this complication, according to Neugebauer. Postoperative hemorrhages are not infrequently noticed after the use of adrenalin, owing to relaxation of the severed vessels.

In the larynx, epinephrin solutions cause an uncomfortable dryness by interfering with the formation of lubricating mucous. This is especially distressing to singers. In the eye their use in scleritis and other disorders may be followed by severe iritis. Instillations of a 1 : 1000 solution in the Eustachian tubes have given rise to violent pain in the middle ear, which was renewed whenever the remedy was thus administered. The use of adrenalin solutions, in the form of a spray at least, is contraindicated in infections, owing to the danger of facilitating the entrance of pathogenic germs into the sinuses.

The rôle I attribute to the adrenal secretion in oxidation, metabolism, and nutrition is as applicable to the untoward phenomena as it was to the therapeutic action of the drug. Following the course of events from start to finish, we have at first the effects of excessive metabolism in all tissues: in the cerebrospinal system, excitement; in the muscles, tremor; in the kidneys, polyuria; in the myocardium, violent contractions (palpitations); in the muscular coats of the vascular system, a marked rise of the blood-pressure. The latter in turn aggravates the process by causing congestion and engorgement of the capillaries (which are not, like the arteries, provided with a muscular coat) of all organs, including the lungs, causing edema of these structures and dyspnea. As the contraction of the arteries proceeds, the aorta has to bear the brunt of the centrifugal pressure, giving rise to marked substernal pain. When it becomes such that the arterioles obstruct the circulation the lethal phenomena are initiated: the pulmonary circulation being impeded, oxygenation fails to occur,

asphyxia follows, and, the myocardium receiving too little blood to sustain its contractile power, the heart, already hampered by the pulmonary congestion, ceases to beat.

In *chronic adrenalism* the same interpretation obtains, the cardiac phenomena being ascribable mainly to the extra work imposed upon the heart by the resistance of the general vascular tension. The gain in weight is a normal result of increased metabolic activity, *i.e.,* overnutrition.

After *local applications* the morbid effects are all the result of the action of the adrenal principle upon the vessels.

The dryness produced by solutions sprayed into the larynx is due to deficiency of blood supplied to the acini and the resulting inhibition of their function. If this is kept up by repeated applications, the tissues, no longer nourished, may slough off, as has been noticed in the upper respiratory tract of aged subjects. The edema observed in this location is not active, as it is in the lungs, but passive, *i.e.,* due to exaggerated relaxation of the vessels after the intense constriction to which the drug had subjected them. This applies equally well to postoperative hemorrhage, and to the severe pain (due to passive congestion) in the middle ear after instillations in the Eustachian orifice.

THERAPEUTICS.—Addison's **Disease.**—Textbooks of practice and therapeutics now teach pretty generally that adrenal preparations are of value in Addison's disease. A personal study of the literature of the subject showed that out of 120 cases treated by adrenal preparations 25 had been sufficiently benefited to be restored to health—as far, at least, as the loss of

adrenal tissue incurred through the local morbid process would permit.

The one great factor in the treatment of this affection by means of adrenal extractives is to drop their *empirical* use, and it is only (and this applies to the use of any disease) when the importance of this fact will have been thoroughly grasped that the proportion of recoveries will be materially increased. Empiricism here may entail death.

[E. W. Adams (Practitioner, Oct., 1903) refers to a group of 7 cases found by him in literature "in which alarming or fatal results were presumably or possibly due to the treatment." He mentions, for instance, 2 cases reported by a prominent clinician treated with "suprarenal gland extract." The chart notes of the cases include the laconic words: "Alarming collapse. One of the cases began to improve markedly when the extract was stopped." In the original paper reference is made to another case treated by suprarenal extract in which "similar collapse was noted." The dose was not mentioned. Such cases are apt to be regarded as examples of the sudden death sometimes observed in Addison's disease, to which Addison himself, Dieulafoy, Anderson, Bradbury, and others have called attention; but this explanation does not hold. Guiol (Bull. de la Soc. médico-chir. du Var., Dec., 1906), having observed similar signs of intoxication and collapse, tried the "remedy"' in a normal subject and obtained the same morbid phenomena. Here, again, we are dealing with fatalities which occurred when the physiological functions of the organs, and, therefore, their mode of action as a therapeutic agent, were but slightly known. C. E. DE M. S.]

The salient guides in the use of these preparations are the *low temperature,* which denotes deficient oxidation and metabolism, and the *weak pulse,* which points to a low vascular tension and inadequate cardiac dynamism. Improvement of a given case is indicated by a gradual resumption of normal

conditions in these two directions, and by the return of bodily vigor, with more or less fading of the pigmentation. As a rule, the more these various morbid phenomena are marked, the larger will be the initial dose required. In other words, marked hypothermia, a very feeble pulse, advanced bronzing, and great debility will indicate that a mere vestige of both adrenals is still active; the dose indicated, then, is that which will supply enough additional principle to *raise the temperature and the blood-pressure to normal,* but *not beyond.* A study of the 120 above-mentioned cases has shown that 3 grains (0.2 Gm.) of the desiccated gland three times daily was the most satisfactory dose to start with. If this fails to raise the temperature and the pulse tension or improve the case, the dose should be increased by 1 grain *per day* until it does, the case being watched closely. As soon as the normal temperature is reached, the dose should no longer be increased, unless a tendency to recurrence of the hypothermia (gradually as the adrenals are being destroyed by the local morbid process) should render it necessary. In less advanced cases the initial doses should be correspondingly small, 2 or even 1 grain of the extract being administered three times daily, the dose decreasing in proportion as the disease is less advanced.

Can we expect a cure from adrenal preparations? In most cases of Addison's disease the local process is tubercular—often limited to the adrenals. A number of examples suggest, however, that the tubercular process itself was benefited, and even cured, by the use of adrenal extract. It is always well, however, to treat simultaneously the tuberculosis on general lines.

The writer observed a case due to adrenal tuberculosis which showed that marked increase in vitality and strength may be secured by suprarenal extract without as great an increase in the blood-pressure as would be expected. Judson Daland (Endocrinology, July-Sept., 1918).

A number of cases are on record in which, after apparent recovery, the cases died suddenly soon after ceasing the use of adrenal preparations. It is evident that even the possibility of curing the morbid process in the adrenals does not replace the destroyed adrenal tissue. It is here that grafting would be of curative value, but only provided *small fragments of adrenal tissue* be inserted, and gradually increased in number until the temperature and pulse indicate that compensation for the functionless areas in the adrenals has been increased

The 120 cases analyzed showed also, and my own experience has further demonstrated, that what is generally known as "adrenal extract," but which, in reality, is the desiccated adrenal gland (the *glandulæ suprarenales siccæ* of the U. S. P.), is by far the most satisfactory agent to use. Injections of adrenal fluidextracts are exceedingly painful—a fact which compromises the issue by introducing the element of shock—while the active principle, epinephrin, adrenalin, etc., sometimes fails altogether to act.

See, also Addison's Disease, Treatment of, this volume.

Shock, Collapse, and Surgical Diseases.—This is another condition in which adrenal preparations show prominently their influence on metabolism. The function I ascribe to the adrenal secretion (to take up the oxygen of the air, and be carried to the tissues where its active principle aug-

ments greatly the activity of this gas) involves the conclusion that it is a prominent factor in the sustenance of the body heat, a fact demonstrated by Reichert, Lépine, Morel, and others. Now, Kinnaman, in a comprehensive study of the temperature relationship to shock, concluded that as shock increased in severity the most uniform progressive factor was the fall in temperature. He states that "in one series [of cases] the fall in temperature was the sole cause of shock." The results of Crile with adrenalin in salt solution given very slowly and gradually for a considerable time thus find a normal explanation in my interpretation of the rôle of the adrenal secretion. He supplied the organism precisely with the substance which sustains the vital process in the tissue-cells. Indeed, he resuscitated animals in this manner—with simultaneous artificial respiration—fifteen minutes after all signs of life had ceased, and was able to keep a decapitated dog alive over ten hours by this same procedure. That it was because the adrenal secretion is able to sustain tissue metabolism, i.e., the vital process itself, that such results were obtained seems self-evident.

In the great war, most of the wounded arrived in a more or less pronounced state of **shock** and needed some restorative before being operated upon. The writer has used adrenalin in saline solution with good results. A half milligram ($\frac{1}{120}$ grain) of adrenalin is mixed with 500 Gm. (1 pint) of saline solution and every patient in shock is injected with 500 Gm. (1 pint) of this mixture. Immediately after operation a second injection is made and 2 injections per day are given for several days; generally, however, it is not needed after 2 or 3 days. The effects are marked increase in blood-pressure and a more ample pulse as well as improve-

ment in the general condition. Dupont (Arch. de méd. et pharm. mil., lxiv, 542, 1915).

The rate of output of adrenalin in dogs and cats, after the blood-pressure had been permanently lowered by exposure and manipulation of the intestines, by partial occlusion of the inferior vena cava, by hemorrhage and by "peptone" injection, was found by the writers to be the same as before the lowering of the blood-pressure, within the limits of error of the methods used for assaying the epinephrin. A marked increase in the rate of output of adrenalin was produced by strychnine. Stewart and Rogoff (Amer. Jour. Physiol., Feb. 1, 1919).

This applies not only to shock, but also to **surgical heart-failure, collapse** from hemorrhage, **asphyxia,** and **submersion.** The adrenal principle (suprarenalin, adrenalin, etc.) promotes energetically, as a catalyzer and constituent of the hemoglobin, the intake of oxygen and its utilization by the tissue-cells, including the muscular elements of the cardiovascular system, and thus causes them to resume their vital activity. It should be very slowly administered intravenously, 5 minims of the 1000 solution to the pint of warm (105° F.) saline solution. In urgent cases 10 drops of suprarenalin or adrenalin in 1 dram of saline solution can be used instead, and repeated at intervals until the heart responds. Artificial respiration hastens its effects.

In **collapse** from weakness of the vasomotor center, such as is liable in **pneumonia, diphtheria,** and **peritonitis,** good results may be obtained with a suprarenal preparation injected into a vein, or, diluted with salt solution, injected subcutaneously. Case of uncomplicated **ileus** in which by this means it proved possible to tide the apparently moribund patient past the danger stage after two days

of fecal vomiting, and thus permitted a successful operation. Heidenhain (Deut. Zeit. f. Chir., April, 1910).

Research showing that epinephrin has no cumulative action. Its action only on direct contact. The continual infusion of a weak solution of epinephrin may prove a useful measure in therapeutics. It is thus possible to send the solution continuously into a vein and thus keep up the blood-pressure permanently while this is being done—the effect being dependent on the concentration of the solution, not on the absolute amount of epinephrin infused. Straub (Münch. med. Woch., June 27, 1911).

During the war the writer in 1 year encountered 15 cases of what seemed to be Addison's disease, in men in active service, except that it displayed a tendency to spontaneous subsidence, even in apparently the gravest cases. A few weeks of rest and quiet, abstention from meat, and treatment with suprarenal extract soon banished all the symptoms. In two of the cases there was what Loeper has described as suprarenal dyspepsia, notably improved by epinephrin. The symptoms developed in all after a period of exhausting fatigue, an infectious disease, or gassing. The asthenia was the most striking symptom, more mental than physical. For months the men were incapable of reading a paper, writing a letter or even answering questions that required any thought. Improvement in this respect was rapid under epinephrin treatment. The blood-pressure was low, but this is common among all the men at the front. A certain tendency to bronzing of the skin was perceptible in all the 15 cases.

The suprarenals, after the patient's recovery are left below par, and resumption of active service is extremely likely to rearouse the old trouble, and the next time it might prove grave beyond recuperation. Carles (Jour de Méd. de Bordeaux, July, 1918).

Reference was made under "Untoward Effects" to the dangers attending the use of the adrenal principles in **surgery** to produce ischemia at the seat of operation. Though such effects are not often met with, the fact remains that they should be borne in mind and the principle that it is the free dilution of epinephrin, adrenalin, etc., that promotes safety. Surgical operations can also be performed without loss of blood, except from the larger vessels, in almost any organ by injecting locally 8 to 10 minims of a 1 : 1000 solution in four or five times the same quantity of saline solution. Care should be taken not to inject too large a dose lest the untoward effects described earlier in this article occur. Solutions of 1 :10,-000 or even 1 : 100,000 are quite sufficient sometimes to produce a bloodless field by causing local constriction of the blood-vessels.

Toxemias and Bacterial Infections. —This is a recent and important development of organotherapy. Abelous and Langlois, Charrin, Oppenheim, and others have laid stress on the antitoxic functions. The process through which this protective rôle was carried out by these organs being admittedly unknown, I submitted in 1903 and 1907 ("Internal Secretions") evidence tending to show that the adrenals and thyroid were the sources of two substances as prominent agents in the immunizing process—the thyroid carrying out, we have seen, the rôle of opsonin (confirmed by Fassin, Stepanoff, and Marbé), while the adrenal secretion acted as amboceptor. While I do not regard these two agents as the sole participants in the immunizing

process, the fact remains that the addition of either of them to the blood enhances to a certain extent its functional activity. Especially is this the case in view of the fact that adrenal secretion, as previously stated, serves to sustain oxidation and tissue metabolism. By doing so it activates the functions of all tissues, including those concerned with the production of protective substances. The blood thus finds itself richer in these substances and more active as a germicidal and antitoxic agent.

> Infectious diseases constitute the principal field in which the adrenalin treatment is of service, and the writer has employed adrenalin successfully in many cases of severe collapse in connection with scarlet fever, pneumonia, and typhoid fever. He does not hesitate to use large doses. He invariably administers it by subcutaneous injection and has observed no after-effects. Kirchheim (Münch. med. Woch., Dec. 20, 1910).
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> Adrenalin, injected intravenously, in saline solution, is indicated in the treatment of peritonitis, used continuously. The action of adrenalin on the diseased organism must be borne in mind. By using the drug in very dilute solution weakened systole becomes strengthened and in time becomes normal in force. The weakened heart and lowered blood-pressure of peritonitis, also due to a toxic substance, indicate the same measure. Holzbach (Münch. med. Woch., May 23, 1911).
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> One c.c. (16 minims) of adrenalin injected subcutaneously in acute infections, typhoid, pneumonia, etc., was found by the writer to cause a sudden rise of pressure with but a slight increase of the amplitude of the pulse; 0.75 c.c. (12 minims) produced less rise in pressure but greater pulse amplitude both on account of increased systolic and lowered diastolic pressure; 0.5 c.c. (8 minims) did not apparently cause any constriction

of the peripheral blood-vessels, but by dilating the venous system and acting on the nerve mechanism of the heart, it improved the venous circulation and consequently the nutrition of the heart. The large doses may be used promptly in postoperative shock, collapse, or acute poisoning; otherwise the smaller doses are safer and productive of better results. S. M. Mansvetova (Roussky Vratch, June 21, 1914).

Epinephrin or adrenalin may be used advantageously in infectious diseases, but to avoid untoward effects it is best given well diluted—10 to 15 drops of the 1 : 1000 solution in not less than 1 dram of water, administered very slowly. If given intravenously it is preferable to administer the saline solution as usual, and then to introduce the needle of the hypodermic syringe into the rubber pipe, injecting a drop of the adrenal active principle (preferably supracapsulin 1 : 1000) into the stream of saline solution at short intervals. In this manner much more adrenal principle can be introduced with a minimum of danger.

> The writers relate the following cases: Man, aged 44, had recently gone through an attack of quinsy, after which he suffered from what was regarded as lumbago. The next symptoms were those of probable malignant disease of the left side of the neck—a parent lesion and enlarged regional lymphnodes. He also began to emaciate without apparent cause, which reinforced the diagnosis of malignancy. It was thought that the tumor in the neck was a secondary nodule, but no primary growth could be detected anywhere. The remainder of the finds of a systematic examination were also negative with the exception of vascular hypotension. This first drew attention to the adrenals and Sergent's white line was repeatedly obtained. Poultices ap-

plied to the loins brought out a brown pigmentation. An injection of adrenalin increased the blood-pressure without causing glycosuria. The lumbalgia had persisted. The patient was interned technically for a slight bronchitis, but in the hospital he rapidly sank and died of adynamia. Autopsy revealed a complication of affections, the primary growth being an ulcer of the base of the tongue with numerous metastases, including the visible ones of the neck. The right adrenal was the seat of a cancerous metastasis, while its fellow appeared to be hypertrophied. The second patient was a man of 24 years, who went through a typhoid fever complicated with perforation and peritonitis. Owing to the profound state of depression, a surgical operation was out of the question. The presence of the white line and low blood-pressure showed the condition of the adrenal functions. Death was preceded by the development of acute hemorrhagic diathesis. There was a marked anatomical foundation for the adrenal insufficiency, but the lesions could not be interpreted beyond evidences of degeneration of some sort. Such lesions have frequently been encountered in death from acute infectious diseases, but the rationale is not apparent, although the adrenals have evidently lost most of their lipoid content. Betchov and Demole (Revue med. de la Suisse Romande, June, 1918).

The recognition of the antitoxic property of the adrenal active principle has recently caused it to be employed as an antidote in **strychnine poisoning,** a fact pointed out by Abelous and Langlois in 1898. These authors also found it to oppose the toxicity of **nicotine,** while Oppenheim obtained similar results with **phosphorus.**

Exner has shown that intraperitoneal injections of adrenalin diminish the rate of absorption of **strychnine** intro-

duced into the stomach, and the writer, therefore, decided to try whether adrenalin given by the mouth would exert a similar effect. He first found that adrenalin could exert its vasoconstrictor action after the arteriolar wall has been subjected to the action of **cyanide of potassium,** and then studied its effects upon rabbits poisoned by the cyanide. He was able to bring about recovery after longer periods than in rabbits which had not received adrenalin. He recommended the following procedure for cases of **cyanide poisoning** in man. Adrenalin should be given immediately, 9 c.c. (*i.e.,* 3 drams) of the 1 : 1000 solution diluted to 90 c.c. saline solution; then Martin and O'Brien's antidote if available. This consists of 30 c.c. (1 ounce) of a 23 per cent. solution of ferrous sulphate, 30 c.c. of 5 per cent. solution of caustic potash, and 2 Gm. (30 grains) of magnesia. The first two solutions should be kept in hermetically sealed phials. The three substances should be mixed when required and immediately taken. The principle of the method is the formation of Prussian blue, which is practically innocuous. The stomach should then be washed out and a further dose of about 5 c.c. (1½ drams) of 1 : 1000 adrenalin solution diluted to 50 c.c. should be given. A brisk saline purge is also recommended, to be administered soon afterward. J. L. Jona (Intercol. Med. Jour. of Austral., July 20, 1909).

Adrenalin found experimentally to counteract the toxic symptoms induced by **strychnine** in the frog. Similarly, if adrenalin and strychnine are injected, guinea-pigs will tolerate several times the fatal dose of the latter drug. The action of adrenalin is actually antagonistic and not dependent on vascular contraction, with slower absorption, as some authors claim, since other poisons are not affected in their toxicity. The antagonism is very similar to that between atropine and muscarine. Falta and Svcovic (Berl. klin. Woch., Oct. 25, 1909; Merck's Archives, Jan., 1910).

Postoperative Intestinal Atony.— To the adrenals seem also to belong the credit of offering the opportunity to antagonize this disorder. When in 1903 I submitted the opinion that the thyroid secretion enhanced the activity of the adrenals—a view since sustained by several experimenters—and that the adrenal secretion on the other hand, influenced the functional activity of the pancreas, pituitary body, and other organs, the statement created some surprise. This feeling died out, however, when, three years later, Starling termed *hormones* a group of substances secreted by various organs which could enhance the functions of other organs. Precisely as I had previously held, these hormones were secreted, according to Starling, by the organs which produced them in the course of their normal functions, and reached the distant structures they influenced through the intermediary of the blood. What I termed the *adrenal system* owed in great part its functional activity to this chemical co-ordination: the adrenal secretion being especially prominent in the process owing to the function I attributed to it, viz., to sustain oxidation and metabolism as a constituent of the hemoglobin molecule.

Bayliss and Starling termed *secretin* a hormone formed in the intestinal mucous membrane under the influence of the hydrochloric acid from the stomach, which is the chemical excitant of the pancreatic secretion. Now, from my viewpoint, this is not a specific excitant; I showed in 1907 (vol. ii, "Internal Secretions," p. 861) that it presented several of the properties of adrenal extractives. We are dealing, therefore, not with a local product, but with a component of all tissues (being as such what Starling has termed a "mamma hormone"), and which when present in unusual quantities in any organ is capable of enhancing correspondingly its functional activity owing to its influence on local oxidation and metabolism.

Another hormone has been obtained from the gastric mucosa by Dohon, Marxer, and Zuelzer (Berl. klin. Woch., Nu. 46, 1908), which was found to enhance intestinal peristalsis. But inasmuch as it is (from my viewpoint) a ubiquitous component of all tissues, and the difficulty of collecting it during digestion being obvious, search for it elsewhere suggested itself. It was found in ample quantities in the spleen—that junkshop in which red corpuscles (which, as I suggested in 1903, are the common carriers of the adrenal principle) are broken up along with other cells. That the splenic hormone referred to is not purely the adrenalin-laden albuminous constituent of the hemoglobin derived from red corpuscles is self-evident, since leucocytes with their nucleoproteid granulations, their trypsin-like cytase, and other ferments are also broken up in the spleen. The fact remains, however, that this splenic hormone specifically stimulates intestinal peristalsis to a degree so remarkable experimentally that it may be readily seen in the exposed intestine of experimental animals ten to fifteen minutes after an intravenous injection.

The applications of this peristaltic hormone in surgery are mainly in those conditions of intestinal paresis following operations on the intestine, and particularly where purgatives,

castor oil included, bring on no results. It is also indicated in all forms of stubborn constipation due to intestinal atony.

Miscellaneous Disorders.—The foregoing disorders may be said to represent those in which adrenal preparations are more effective than any other preparation at our disposal. There are several others, however, in which they will probably prove of considerable value, when sufficient trial of them in practice will have warranted a final pronouncement. These are:—

Hemorrhage from the pharyngeal, esophageal, gastric, or intestinal mucous membrane. Here the mastication of adrenal substance or the use of powdered adrenal substance in 5-grain capsules arrests the flow, by causing active metabolism in the muscular elements of the arterioles of the mucosa and constriction of these vessels. The active principle, epinephrin, supracapsulin, etc., has also been given by the mouth in 10- to 15- drop doses.

To avoid **hemorrhage** during the removal of placental rests after abortion the writer exposes the cervix and practises deep injection of the following solution into several points of the cervical tissue,—either 1 c.c. of 1 per cent. or 2 c.c. of ½ per cent. cocaine solution to which 3 drops of 1 : 1000 adrenalin solution has been added. After waiting ten minutes, the operation of emptying the uterus is practically bloodless and the organ is firmly contracted, though patency of the cervix remains. O. Grasser (Zentralbl. f. Gynäk., June 19, 1909).

The writer has seen within the past year 5 cases of vicarious **hemorrhage,** 1 of the rectum, from the inner canthus of the nose, etc., in which he prescribed the suprarenal extract—adrenalin 1 : 1000, giving 15 drops every three hours until it ceased—and secured prompt relief. J. W. Irwin (Med. Brief, Aug., 1911).

Spontaneous recurrent **epistaxis** is usually due to ulceration over capillaries or a vessel in the anterior nares, but at times it is difficult to locate the precise area from which the hemorrhage comes. This may be overcome by an application of adrenalin solution to the anterior portion of the septum. This blanches the whole mucosa except at the spots which give rise to the bleeding. These then stand out clearly against the pale surface as red, circular areas. W. Lapat (Jour. Amer. Med. Assoc., lxvii, 1159, 1916).

Asthenic cardiac disorders with **dilatation** of the right ventricle, dyspnea, and possibly cyanosis and edema, owing to the direct action of the adrenal principle on the right ventricle and improved oxidation and metabolism in the cardiovascular muscles and the tissues at large. Tablets of from ½ to 1 grain of the desiccated gland can be taken after meals.

Adrenalin caused in the terrapin a disappearance or a diminution in the tonus waves observed in the sino-auricular muscle preparation, and a simultaneous increase in the force and amplitude of the contraction, and in some instances an increase in the rate of contraction. When the solution was strong, the waves ceased almost immediately; when a more dilute solution was used, only a few tonus waves appeared after the addition of the adrenalin to the Ringer's solution. The length of time required after an injection of adrenalin, before the recurrence of the waves, varied directly with the strength of the adrenalin solution used. Oxygen added to Ringer's fluid seemed to hasten the process of recovery, which might be only a matter of hastening the oxidation of the adrenalin. Gruber and Markel (Jour. of Pharm. and Exper. Therap., Aug., 1918).

The writer tested the effect of the injection of 0.5 c.c. (8 minims) of a 1 : 1000 solution of adrenalin in normal soldiers and in soldiers suffering

from "irritable heart." In only 1 of the 27 control cases was there a suggestion of hypersusceptibility to epinephrin. In 65 patients the epinephrin test was positive in 39, doubtful in 6 and negative in 19. The most important symptoms of the reaction were the presence of tremors, sweating, flushing, pulsation of peripheral blood-vessels, general nervousness and increase in blood-pressure, pulse-rate and depth of respiration. Furthermore, the "irritable heart" cases showed an increase in basal metabolism and in blood sugar more marked than in normal individuals. The electrocardiogram showed most constantly a slight decrease of the height of the T-wave. In individual cases other abnormalities were seen, such as increase of sinus arrhythmia, prolongation of P-R interval, partial heart block, inversion of the T-wave and the production of ventricular extrasystoles. The writer advises the use of epinephrin as an aid in the diagnosis of "irritable heart." Peabody (Jour. Amer. Med. Assoc., lxxi, 1912, 1918).

Asthma.—To arrest the paroxysms, by augmenting the pulmonary and tissue intake of oxygen and the cardiovascular propulsion of arterial blood. From 5 to 10 minims of the 1 : 1000 solution of adrenalin in 1 syringeful of saline solution should be injected hypodermically, very slowly, massaging the part so as to insure absorption of the solution.

[The effect is so rapidly obtained and satisfactory that the patient is sometimes entrusted with a syringe and allowed to treat himself. But this is a dangerous procedure. I have observed, in consultation, a death which could undoubtedly be attributed to this cause. C. E. de M. S.]

Case in which alarming manifestations were produced by the hypodermic administration of adrenalin. The man became cyanotic and had the most severe rigors the writer had ever seen; but the **asthmatic attack**

was immediately relieved. After subsidence of the rigor the only ill effect was muscular soreness for 24 hours. S. J. Meyers (Miss. Valley Med. Jour., Nov., 1917).

Effusions.—To prevent the recurrence of serous effusions in the pleura, the peritoneum, the tunica vaginalis, etc., after aspiration, by reducing the permeability of the local capillaries and restoring the circulatory equilibrium. From 8 minims to 2 drams (according to the size of the cavity) of suprarenalin or adrenalin, in four times the quantity of saline solution, should be injected into the cavity.

Disorders of Pregnancy and Parturition.—The most useful employment of adrenal preparations in disorders of this class is in **obstinate vomiting of pregnancy.** This was suggested by the frequency and obstinacy of vomiting in Addison's disease and the beneficial influence of adrenal gland over this symptom. The benefit is probably due to the more active destruction of toxic wastes—which are increased during pregnancy owing to the presence of the fetus—a function in which we have seen the adrenals take part.

Severe case of **hyperemesis gravidarum** of more than two months' duration treated with marked success by means of adrenalin in small doses. Various remedies had been tried, and artificially induced labor was seriously contemplated. S. Rebaudi (Gazz. degli Osped.; Zentralbl. f. Gynäk., Nu. 44, 1909).

Cancer.—The fact that the cancerous growths in mice and rats had been caused to disappear by the injection of the active principle into these growths suggested that the latter might also prove efficacious in man. About all that can be said for the present is that the results warrant further trial.

Second series of experiments in the König Charité on private patients on a larger scale, based on Reicher's experiments in animals. The writer gave to men an average of 0.2 to 0.3 Gm. to begin with and increased up to 1 Gm. of the original solutions of adrenalin, selecting cases which did not suffer from bad heart disease or calcification of arteries. The best results were obtained in a boy of 12 years who suffered from **sarcoma** of the vertex. Within three and a half weeks the tumor was reduced to one-third of its size. The remaining third was made to disappear under the Christian Müller method of X-rays and high frequency combined. Since six months the tumor has undergone complete retrogression; no recurrence has occurred. The writer also reduced temporarily several cases of **malignant lymphoma.**

He has since tried to treat other inoperable tumors, among others a **melanosarcoma,** which was identified as such under the microscope. It was a metastasis in the groin which occurred one and a half years after excision of the primary tumor on the dorsum of the foot. Within one and a half months it had increased to the size of of a man's fist. In three months he was able to reduce its size very little, but, at least, it has become stationary, while before it was growing very rapidly. It is remarkable that during the treatments the patients increased much in weight—up to 14 pounds in his series. There must be a constant anomaly of metabolism somewhere. Reicher (Berl. klin. Woch., Nu. 20, 1911).

The desensitizing of the skin by means of adrenalin permits the use of nearly double the dose of the **X-rays** for a period of from fourteen to eighteen days. The most important indication for this method is the treatment of **malignant tumors** situated subcutaneously. Reicher and Lenz (Münch. med. Woch., June 13, 1911).

Case of squamous-celled **carcinoma of** the **cheek** treated with X-rays and later with radium, with very little, if any, improvement. To assist the penetration of the rays, applications and injections of adrenalin (1:1000) were employed. The injections were discontinued, being followed by local edema, but the applications were continued for some time. Great improvement resulting, a daily dressing of lint soaked in adrenalin solution was applied, the radium treatment being discontinued. The ulcer healed gradually and 6 years later there had been no recurrence. L. C. Peel Ritchie (Lancet, June 29, 1912).

The writer saw benefit follow a single injection of adrenalin in **cancer,** evidently made as a test. Rosenberg was obliged to discontinue adrenalin injections because of the pain caused. Gräffner (Berl. klin. Woch., Nov. 20, 1912).

Case of **carcinoma of** the **tongue,** the size of a hen's egg, which had necessitated tracheotomy, in which the writer tried injecting a few drops of adrenalin, gradually increasing to 2 Gm. (30 grains) a day. The tumor began to undergo gangrene and to be thrown off, the remaining mass being snared off. Holscher (Annales des Mal. de l'Oreille, du Lar., du Nez et du Phar., 7 Liv., 1912).

Case of inoperable **carcinoma of** the **pharynx** with cachexia and swelling of the cervical glands treated with a tabloid containing fresh **thyroid** 6 grains (0.4 Gm.), **adrenal** ¾ grain (0.048 Gm.), **pituitary** ¹⁄₁₆ grain (0.004 Gm.) one night and morning. The improvement was slow but steady. In 4 months, an additional capsule being given daily, she could swallow all foods if well masticated, except meat. In 5 months she resumed work, improving steadily, having considerably increased in weight. J. T. Shirlaw (Liverpool Med.-Chir. Jour., July, 1913).

Osteomalacia.—In osteomalacia the adrenal preparations find a normal indication in view of their stimulating influence on metabolism and, therefore, general nutrition, in which the osseous system must normally partake. This

beneficial process is further enhanced by the fact that the thyroid apparatus is itself stimulated through the same cause, and that the thyroid secretion, as shown by Macallum, Parhon, and others, actively promotes calcium metabolism.

> The writer collected 47 cases treated with adrenalin, 11 pregnant and 35 non-pregnant women. Of the former 45 per cent. were cured and about 18 per cent. improved; of the latter 17 per cent. were cured and 40 per cent. improved. R. Cristofoletti (Gynäk. Rundschau, v, 113; 169, 1911).

LOCAL USE.—To check **hemorrhage** from wounds, adrenalin can be used in various organs.

> In free **hemorrhages** from mucosæ or in simple congestion of the latter, local application of the extract is quite sufficient for hemostasis. In a parenchymatous hemorrhage, in the course of an operation, the indication is filled in the same manner. Satre (Le Prog. Méd., July 8, 1917).

Bates, Dor, and many other ophthalmologists have introduced the local application of a weak solution to the **conjunctiva** to produce a bloodless field, and also to enhance the local effects of cocaine, atropine, eserine, and other agents used in the eye. Weak solutions may also be used in **conjunctivitis.**

> Instillations of 4 to 5 drops of the 1 : 1000 solution of adrenalin or subconjunctival injections of a smaller quantity causes a primary reduction, followed by a marked increase in tension. Subsequently there is a secondary reduction of tension. These changes are observed in normal as well as glaucomatous eyes. The reaction in normal eyes is not very great, but in glaucomatous eyes it is quite marked. In normal eyes, the effect of the adrenalin passes away in a few hours, whereas in glaucomatous eyes the effect continues for several days.

> In a certain number of cases of **glaucoma** the adrenalin produced a lowering of tension, whereas in others it caused attacks of acute exacerbation. Repeated instillations in normal eyes are apparently without much effect, but in glaucomatous eyes there is a marked increase in tension after the final instillation. The result of the combined use of eserine and adrenalin on tension indicate the two opposing forces are at work. Therefore, in eyes that have a predisposition to glaucoma it is advisable to combine eserine with the adrenalin. J. Rubert (Zeit. f. Augenheilk., Bd. xxi, S. 97, 224, 1909).

> In 50 cases of **conjunctival hyperemia** from causes varying in nature from simple congestion due to eyestrain to the most severe types of **conjunctivitis,** a single drop of adrenalin chloride solution, 1 : 5000, in the conjunctival sac almost immediately caused a blanching of the membrane, commencing in about ten seconds, and reaching a maximum in from five to ten minutes, the effect lasting from one-half to two hours, according to the nature of the case. The blanching effect may be obtained by even a solution of from 1 : 12,000 to 1 : 10,000 in from thirty seconds to two minutes. A solution of 1 : 2000 was found to give the best results in operative work upon the eye, causing no irritation that could be noted upon close observation. A 2 per cent. solution of cocaine hydrochloride was used ten minutes prior to the instillation of the adrenalin, when operation was contemplated, in order that the effect of the anesthetic might not be interfered with, thus insuring a painless and almost bloodless result. MacFarlane (Can. Practitioner, June, 1909).

This applies as well to the local use of adrenal extractives in the **nose, pharynx,** and **larynx,** a weak solution of cocaine, 4 per cent., for example, acquiring the power of 15 to 20 per cent. solution, both as anesthetic and styptic. Combined with B-eucaine (5 c.c. of 1 per cent. solution), supra-

renalin, or adrenalin, 3 drops of the 1:1000 suffice when injected in small quantities into the tissues, or, applied locally to mucous membranes, are quite effective for **operations** in almost any region, including the urethra. The cocaine and adrenalin solution referred to above is equally effective, the operation being performed after three or four minutes. These solutions are extensively used, especially for dental, uterine, rectal, and urethral operations.

Hemorrhoids.—Bouchard introduced the use of tampons soaked in adrenal preparations for the treatment of this condition. In external piles, especially if there is great distention and hemorrhage, 20 drops of suprarenalin in 2 drams of saline solution applied with a compress relieve greatly the congestion and the pain. A small quantity of cocaine enhances these beneficial effects.

> The writer obtained a rapid retraction of **hemorrhoidal tumors** by giving a single injection of 0.5 c.c. (8 minims). This dose will reduce a hemorrhoid the size of a walnut within a week's time. A hemorrhoid the size of an apple was greatly reduced by 15 injections given during 7 weeks. The drug is injected *under the mucosa*, as is done for anesthesia of the mucous membrane. H. Krukenberg (Münch. med. Woch., July 30, 1918).

Neuralgia, Sciatica, and Neuritis. —To subdue and sometimes arrest pain in these disorders, by causing ischemia of the hyperemic and, therefore, oversensitive nerves. One to 2 minims of a 1:1000 suprarenalin or adrenalin ointment applied by inunction over the painful area.

Cutaneous Disorders.—Local applications of the 1:1000 solutions of supracapsulin, adrenalin, etc., may be used advantageously to assuage pain and counteract inflammation, which they do by causing constriction of the arterioles. Among the conditions in which they have proven useful are **toxic erythema, urticaria, acne, sunburn, bee-sting, eczema, chilblains, arthralgia, arthritis, varicose veins, burns, X-ray dermatitis, and herpes zoster.**

> The vasoconstrictor property of epinephrin was taken advantage of by the author in 3 cases of **erythema** of the face ("red nose"), 2 of the patients being young men, and the third a young lady. A solution of epinephrin hydrochloride, 1:1000, was given internally in 5-minim doses in water 3 times daily ½ hour before food, and the treatment continued during 5 to 6 months with short intervals. The erythema almost entirely disappeared, and 1½ years after treatment it had not reappeared. No bad effect on the heart or bloodpressure was observed. Rothmann (Lancet; Charlotte Med. Jour., Oct., 1913).

PITUITARY ORGANOTHERAPY.

"We may assume," wrote Schäfer in 1898, in a review of the investigations on the physiological rôle of this organ, "that the pituitary body furnishes to the blood an internal secretion, and that this internal secretion tends to increase the contraction of the heart and arteries, and perhaps influences nutrition of some of the tissues, especially bone and the tissues of the nervous system." Howell showed, however, that of the two lobes of the organ extract of the anterior lobe produced no effect—a fact confirmed by several investigators—and that the main action of extracts of the posterior lobe was to slow the heart and raise the bloodpressure. Schäfer and Vincent then

concluded, after experiments, that the pituitary contained both a pressor and a depressor substance. The latter effect is increasingly being disregarded in practice, the posterior lobe, now official (U. S. P., 1916), giving rise to pressure effects.

> Doses of 15 to 20 minims of pituitrin produce a perceptible increase in the blood-pressure in from four to twenty minutes, and maintain it from twenty minutes to an hour or even longer, differing in this respect from adrenalin, in which the effect is far more transient. There is a coincident change in the pulse rate, diminishing as the blood-pressure increases and increasing as it falls. However, this change is more gradual, both in its downward course and its return to normal.
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> The rise in blood-pressure varies from 8 to 38 mm., while the pulse rate falls from 4 to 17 beats per minute. No untoward effects were noted in any of the cases in which larger or repeated doses were administered. The inhibitory influence upon the pulse is more lasting than the influence upon the blood-pressure. H. G. Beck and J. J. O'Malley (Amer. Med., Oct., 1909).
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> In animals intravenous injections of pituitrin in small dosage can be repeated at intervals of 10 or 15 minutes without significant failure of their pressor effect in animals. In either the dog or cat occlusion of the adrenal circulation does not diminish the pressor effect of a standard dose of pituitrin. There is probably, therefore, no direct dependence on adrenal functioning upon pituitary secretion. Hoskins and McPeek (Amer. Jour. Physiol., Sept. 2, 1913).
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> The effect of pituitary extract on the human blood was by no means found uniform by the writer, and did not correspond to the striking results obtained in animal experimentation. As previously shown by von der Velden, pituitary extract caused no constant rise in blood-pressure and no change in the pulse-rate or in the respiration-rate. Nor was there any special effect on the general system. Behrenroth (Deut. Archiv f. klin. Med., cxiii, Nu. 3-4, 1914).

The pressor substance was looked upon as resembling that of adrenal extracts, its application to mucous membranes producing blanching, as is the case with adrenalin. With Herring, Schäfer then found that pituitary extract was endowed with powerful diuretic properties, and that it produced dilatation of the organ. Finally, Herring advanced the theory that the secretion was formed in the anterior lobe and completed in the posterior lobe, and that it then passed into the third ventricle, to mix therein with the cerebrospinal fluid.

From my viewpoint, the prevailing idea that either lobe of the pituitary is a secreting organ was based on an assumption at the start, and has been perpetuated as such. The effects of its extracts are those of the adrenal principle which the posterior pituitary contains; not only does the pressor substance give the actions of chromaffin substance, due to the presence of the adrenal principle, but it produces the same effects. The functions I have attributed to the pituitary are totally different; but as they do not bear in any way upon the valuable therapeutic effects of this organ, they need not be described in the present connection. As I view it, therefore, pituitary preparations merely afford an additional and efficacious way of administering adrenal preparations. Being bound up in organic combination, the adrenal principle acts with less violence, owing, probably, to the fact that even in the tissues, after the pituitary preparation has been injected, the product is decomposed very slowly.

The writer found that extract of suprarenal and pituitary glands had a rapid and marked effect as pupil dilators. Thyroid had no mydriatic effect. Catapano (Deut. med. Woch., Jan. 31, 1911).

Comprehensive experiments in dogs led the writers to conclude that pituitrin injected intravenously caused a moderate rise of the blood-pressure, slowing of the pulse rate, and a temporary arrest of the urinary excretion, without true secondary polyuria. The rise in blood-pressure is more marked when the normal tonic activity of the vagi has been suspended or the terminations of this ner e paralyzed. It is due to a visceral and peripheral vasoconstriction, which appears to occur independently of the general vasomotor center. The diminution of urinary excretion produced by pituitrin is dependent upon a renal vasoconstriction which seems to be of peripheral origin. In the whole animal the action of adrenalin is exerted in the same direction as that of pituitrin, but is more powerful and also more evanescent. It differs from pituitrin in increasing the amplitude of, and accelerating the contractions of, the isolated heart. Beco and Plumier (Bull. de l'Acad. de Méd. de Belg., xxvii, No. 5, 1913).

Pituitary extracts, when prepared by certain methods, yield color reactions suggesting epinephrin or an epinephrin-like compound. The physiologic actions of such solutions can be explained by the presence of such a compound, modified by admixed substances. That epinephrin has not yet been isolated from these glands may be due to the small amounts present. Watanabe and Crawford (Jour. of Pharmacol. and Exper. Therap., Jan., 1916).

Whichever opinion ultimately prevails, the fact remains that pituitary is a valuable remedial agent in many disorders. Its marked advantage is that it sustains the rise of blood-pressure, to which it gives rise much longer than

does adrenalin, thus being more reliable in shock and other emergency cases. It seems also to sustain the temperature and the muscular tone, cardiac, vascular, intestinal, and uterine, longer than the adrenal active principle. It possesses also a great practical advantage over adrenalin and other adrenal principles in that it can be administered by the mouth without compromising its effects.

At the present writing (1921) pituitary preparations (posterior lobe) are looked upon as capable of raising the blood-pressure, of enhancing the contractile power of the uterus, and by dilating the renal vessels of producing diuresis.

PREPARATIONS AND DOSE. —Pituitary gland is available in drug stores in the form of powder or tablets of desiccated gland. The new U. S. P. (1916) has made official a powder (*hypophysis sicca*) of the *posterior lobe*, the active one therapeutically, the dose of which is ½ grain (0.03 Gm.). The prevailing tendency is to give too large a dose of pituitary. I have seen very harmful effects produced by such medication. I seldom prescribe over ⅒ grain (0.006 Gm.) three times daily.

A product called "pituitrin" by its manufacturers, in the form of a solution, is available on our market for oral or intramuscular use, the dose of which is given as 10 to 30 minims (0.66 to 2 c.c.).

There is also a liquid extract of the posterior lobe, wrongly termed "infundibular extract," the infundibulum being the pedicle which unites both lobes of the pituitary to the base of the brain. This infundibular extract affects mucous membranes precisely as do adrenal extractives, and should be applied only when diluted in eight or ten

times the same quantity of saline solu-
tion. It may be given orally in 10- to
30- minim (0.62 to 2 c.c.) doses, or
intramuscularly in 3- to 15- minim
(0.2 to 0.92 c.c.) doses.

Liquor hypophysis, U. S. P. (solu-
tion of hypophysis), is a preparation
containing the water-soluble principles
from the fresh posterior lobe of cattle.
It is standardized for uterine activity
on the isolated uterus of the virgin
guinea-pig, and is officially required to
be kept in a sterile condition in glass
containers. Dose, 5 to 15 minims (0.3
to 1 c.c.).

An important addition to our pituitary
pharmacological agents was made re-
cently by Prof. T. B. Robertson of the
University of California and now of the
University of Toronto. He terms **tethelin**
a substance isolated in relatively pure form
from the anterior lobe of ox pituitary. It
was found to retard the early growth of
animals, but to markedly accelerate post-
adolescent growth. The animals receiving
it were smaller but heavier than controls,
and showed favorable effects on their
skins. Animals deprived of food for a
time and then given unlimited food, re-
gained weight more rapidly when given
tethelin than controls. It stimulated the
healing of wounds. The substance has
marked powers in influencing the growths
of tissue. It was given orally and hypo-
dermically with the same results.

THERAPEUTICS. — Acromegaly.
—The possible value of pituitary ex-
tracts here suggested itself, but, al-
though a few of the symptoms, the
headache, lethargy, and amnesia, were
relieved in some, no cures were ob-
tained. Analysis of the cases reported
benefited suggests an explanation apart
from the organ as the source of an in-
ternal secretion, but entirely in keeping
with the presence in the pituitary prep-
aration of adrenal secretion in organic
combination. Marinesco observed that
it was the extremely violent headaches

that were relieved, there being no benefit
otherwise, excepting perhaps increased
diuresis. Kuh, obtaining no favorable
result, withdrew the remedy, but the
patient begged to be given the powders
again, having found his headache much
more intense when he failed to take
them. The same observation had been
recorded by Cyon, the patient, an obese
child of 12 years, having besides lost
twenty pounds in weight. What benefit
was obtained in 1 case out of 7 cases
treated by Kinnicutt was also limited
to the headache and neuralgia. Les-
zynsky, after a prolonged trial in 2
cases, wrote: "While some published
reports as to the efficacy of the prep-
arations of the sheep's gland have
seemed quite encouraging in so far as
the relief of headache and of paresthesia
of the hands is concerned, it is the
general consensus of opinion that it in
no way influences the progress of this
disease."

Still, the relief of the headache and
paresthesiæ indicates some potent ac-
tion. This is accounted for if the adre-
nal principle is considered as the active
agent of the pituitary preparations,
since, as Langley has shown, it is prin-
cipally upon the *arterioles* that the
adrenal principle acts, a view which
has now become classic. Such being
the case, the tumor of the pituitary, or
the compressed tissues around it, re-
ceive less blood through their con-
stricted arterioles, and the sensory ter-
minals of the peripheral likewise. The
resulting ischemia of these tissues thus
accounts for diminution of pain—as
long only as the remedy is administered.

Cardiac Disorders.—As shown by
Rénon and Delille, pituitary gland
raises the depressed arterial tension and
corrects purely functional disorders of
rhythm.

It is recommended in doses ranging from 3 to 6 grains (0.2 to 0.4 Gm.) of the whole gland in myocardial weakness, particularly in that due to infections when the blood-pressure is receding, the pulse is becoming more rapid, and the urine scanty. While less active than digitalis as a diuretic, it, nevertheless, serves a valuable purpose in this connection. It is advantageous in **mitral disorders** when there is hyposystole and in **chronic myocarditis,** particularly that due to alcoholism. It is also useful in the **tachycardia** of certain neuroses and during menopause. These results have been confirmed by Trerotoli, Parisot, and others.

It is contraindicated in aortic affections in any disorder in which high vascular tension prevails, and where there is a tendency to anginal pains, which it tends greatly to aggravate.

Pituitary gland is preferred to adrenal preparations and particularly adrenalin when the action is to be sustained, the former being useful in urgent cases. Rénon and Delille, however, prefer digitalis, and recommend pituitary gland only when the latter fails. Leonard Williams, on the other hand, deems it superior to digitalis, strophanthus, strychnine, and other classic tonics in what he terms the "runaway heart of toxic states," influenza, pneumonia, bronchitis, etc., with tachycardia, but low blood-pressure, and in all cases in which there is posttoxic cardiac debility. In these cases—which, from my viewpoint, are instances of pure hypoadrenia—Williams regards pituitary preparations superior to any remedy at our command.

In **heart-failure** and **shock,** it has been highly recommended, 15 minims (0.92 c.c.) of the extract being injected intramuscularly. While its virtues would seem to recommend it for the perpetuation of the effects of adrenalin, which are, at best, but temporary, the number of cases in which it has been tried has been too limited so far to warrant an opinion as to its actual value.

In 3 cases of **heart-failure** during **anesthesia** the writer injected 1 c.c. of a 20 per cent. solution of the posterior lobe of the pituitary body intramuscularly. The effect was almost immediate, and the almost imperceptible pulse soon became large and bounding. This effect lasted from twelve to sixteen hours, and gradually passed off. Not only did the pulse become larger in expansion, but it was also slowed, and, whereas it had been irregular, it became regular. This effect seems due not only to the action of the drug on the blood-vessels, but also on the heart. The injection was given in conjunction with normal saline by rectum. G. G. Wray (Brit. Med. Jour., Dec. 18, 1909).

The benefit which follows the use of pituitrin by intramuscular injection when the blood-pressure is abnormally low is very marked. The writer recommends it especially for **threatened collapse** and **hemorrhage after childbirth.** He thinks it may prove of value in **surgical shock** and in **acute febrile states,** but his use of it in these cases has not yet been extensive. Pituitrin has two advantages over adrenalin: namely, its action is moderate and prolonged. Klotz (Münch. med. Woch., May 23, 1911).

While the treatment of **low blood-pressure in infectious diseases** by injections of adrenalin is very successful, it is not perfectly satisfactory, Staub having shown that only 6 per cent. of the drug reaches the circulating blood, while the remainder is disintegrated at the site of injection, while large doses may cause suppuration, and even extensive necrosis of the skin at the site of injection and also glycosuria. The author has, therefore, substituted pituitrin on ac-

count of its powerful action on unstriated muscle. H. von Willebrand (Finska laekere Handl., vol. liv, 1912).

The writer recommends pituitrin in **acute heart failure with dilatation.** Too large a dose may in the aged result, however, in a sudden harmful rise of pressure. This may entail hemorrhage and apoplexy. A weakened and tired-out myocardium may be rapidly reduced to a normal size. E. Zueblin (Boston Med. and Surg. Jour., Dec. 24, 1914)).

After using posterior pituitary (pituitrin) in over 1000 cases with **cardiovascular** and **metabolic atony** and **deficient defensive activity** the writer regards pituitary therapeutics as easily the most effective resources at our command in organotherapy. R. A. Bate (Louisville Mthly. Jour. of Med. and Surg., Sept., 1915).

Obstetrics.—Dale found, in the course of comprehensive experiments, that (in keeping with that of the adrenal principle) the action of extract of pituitary was "a direct stimulation of involuntary muscle without any relation to innervation." Fröhlich and Frankl-Hochwart then ascertained that it caused contractions of the pregnant uterus in rabbits, while Foges and Hofstätter resorted to this property in so far as the human uterus was concerned to check post-partum and other uterine hemorrhages, the test including 63 cases. The extract proved worthless by the mouth; but when injected intramuscularly, marked uterine contraction appeared within five minutes and lasted a long while in most cases. It is especially efficient in **placenta prævia,** particularly after version and expulsion of the fetus, removal of the placenta is accompanied by **profuse hemorrhage.** It is also useful in cases of normal labor followed by **hemorrhage** or **uterine relaxation.**

In 63 cases of **post-partum hemorrhage** and after 1 **abortion** the intramuscular injection of pituitrin (in doses of 1 to 2 c.c.) proved superior to ergotin with reference to the intensity of the contraction and continuance of the excitability. The authors were enabled to note the effect of pituitrin particularly in 6 cases of extraperitoneal Cesarean section. "After not more than five minutes one could see how the exposed uterus contracted, in response to a light tactile irritation, to a firm ball. The action continued for a long time, which accounts for the fact that there was no hemorrhage, a complication that is always feared in connection with Cesarean section." In accordance with their observations, the authors are of the opinion that there is no doubt concerning the specific effect of pituitrin upon the excitation of the uterus. Foges and Hofstätter (Zentralbl. f. Gynäk., Nu. 46, 1910).

Pituitary liquid in **placenta previa,** in ½ c.c. (8 minims) dosage, with advisable repetitions during the latter part of the first stage, and a single large dose (1 to 1½ c.c.—16 to 24 minims) when dilatation is complete, is recommended by the writers, their results having been uniformly good. Gallagher and Gallagher (Surg., Gynec. and Obstet.; Amer. Med., Dec., 1916).

Small doses of pituitary **extract** without any curettement or packing are recommended by the writer in **incomplete abortion** and **placenta previa.** He usually gives ½ c.c. (8 minims) pituitary liquid hypodermically daily or every other day until the placenta is expelled. This occurred in most cases in 2 or 3 days and in but 1 in 5 days. The bleeding during the time does not exceed that of an ordinary menstrual period. Lipkins (N. W. Med., Mar., 1918).

The trend of recent clinical observations is that if pituitrin is used at all in obstetrics, it should be in smaller doses even in cases of uterine inertia, full doses exposing the uterus to rup-

ture and the fetus to asphyxia. It is especially dangerous in primiparæ.

A case was observed in which after evacuation of the uterus after abortion, pituitary and ergotin were given for hemostasis. The pulse became very poor and soon afterwards the woman collapsed. Hemorrhage had wholly ceased. Intravenous saline infusion alone produced a reaction, but only after some hours. The condition is best explained by synergism of 2 drugs which alike cause excessive contraction of the blood-vessels facilitated by the great loss of blood. Bovermann (Münch. med. Woch., July 9, 16, 1912).

The following complications have followed the use of pituitary extract in labor cases: Post partum uterine atony, fetal asphyxia, maternal collapse, eclamptic convulsions, tetanus of the uterus, premature placental separation and rupture of the uterus. In his own experience uterine tetanus followed as little as 5 minims (0.3 c.c.) of the extract in 2 instances. A greater tendency to tetanus in primiparæ than in multiparæ was noticed, and in many instances restoration of normal contractions did not follow, a low forceps operation becoming necessary. Fetal asphyxia was likewise noted in many primiparæ, though never fatal. Post partum atony, with alarming hemorrhage in several cases, was noted particularly in prolonged labor and in multiparæ in whom several pregnancies had occurred in rapid succession. The drug has no place in normal obstetrics. L. G. McNeile (Amer. Jour. of Obstet., Sept., 1916).

Within 12 weeks of each other there had been admitted to the obstetric ward of the Delaware Hospital 2 patients with spontaneous rupture of the uterus, following the administration of a single dose of 1 c.c. (16 minims) of pituitary solution. They had met the usual indications for the use of pituitary solution. Both pelves were practically normal and the conjugata vera, as estimated at operation, at least 10 cm. in each. But both babies were found to be somewhat above the average size, one weighing a little above and the other a little below 4500 Gm.—9.9 pounds. One patient died, the other recovered. W. Wertenbaker (Jour. Amer. Med. Assoc., lxviii, 1895, 1917).

After testing pituitrin in a large number of **labors,** the writers advocate very small doses by the intramuscular injections, their average dose being 2 to 4 minims (0.12 to 0.25 c.c.), and in labor at term exclusively—never for the induction of abortion or premature labor, where it fails entirely. It is only indicated after the onset of labor for strengthening the uterine contractions; also in combination with castor oil for the induction of labor at full term. These small, entirely harmless doses of pituitrin serve to reduce the need for the application of forceps, thus causing otherwise instrumental deliveries to terminate like normal progressive labors. Stein and Dover (Med. Rec., Aug. 11, 1917).

Analyses of the reports of 5245 cases of **labor** in which pituitrin was used strikingly emphasized the fact that the contents of 1 ampoule (15 minims—1 c.c.) is much too large a dose and that this should be reduced to ⅓ of that dose, which may be repeated at intervals of 30 to 50 minutes if necessary. The first dose is usually decidedly more effective than the subsequent ones. The field of usefulness for this drug is sharply limited. This is secondary inertia late in the second stage in multiparous women who have had previous unobstructed labors, a normal presentation, fully dilated cervix, head moulded and through the brim, membranes ruptured, and perineum relaxed. In such cases its use frequently avoids a low forceps operation. An anesthetic should be given when the action of the pituitary extract begins, and one should always be prepared to complete delivery with forceps. It is inferior to ergot for the control of postpartum hemor-

rhage. It should never be used in normal labor and it is dangerous in primiparæ. Its use should invariably be preceded by accurate pelvimetry. In the cases analyzed there were 20 of rupture of the uterus, 12 in the last year in a total of 1293 cases in which the drug was used. This gives 1 in each 106 cases. The danger to the fetus has increased during the past year, probably owing to the more reckless use of large doses. During 1914 there were 27 fetal deaths in 3952 cases, or 1 in 146 cases, while during 1916 there were 34 fetal deaths in 1293 cases, or 1 in every 38 cases. Dangerous fetal asphyxia is even more frequent. It is quite obvious that the field of safe usefulness of pituitary solution is very sharply limited and any transgression is fraught with considerable danger. J. J. Mundell (Jour. Amer. Med. Assoc., June 2, 1917).

Indications for use of pituitrin are limited to simple **uterine inertia** in multiparæ without fetal or maternal dystocia and in patients not exhausted. The author's personal experience and observations of cases referred to the Lying-In Hospital, had led him to add his own to the warnings already published. Pituitrin in Cesarean section is not as certain as ergot. It is merely an aid to forceps in certain cases of dystocia where stimulation of the uterine contractions might drive the head to a more suitable level for instrumental delivery. Pituitrin was of especial value in curettage for incomplete abortion, also useful in metrorrhagia of young girls and in older women with small fibroids or inflammatory lesions in the adnexal regions resulting in hyperemia. G. W. Kosmak (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 29, 1918).

The writer has long opposed the use of pituitary in labor. Further experience has confirmed the opinion. Rupture of the uterus and laceration of the cervix has followed improper use of the drug. Asphyxia of the newborn has been caused and the en-

docrinal relationships of the fetus have been disturbed. As to the use of the drug in cases of Cesarean section, it should not be given after the sutures were put in, as the sudden contraction may tear the sutures out, and peritonitis follow. In true primary inertia with or without rupture of the waters pituitrin may do good. J. B. DeLee (Trans. Amer. Med. Assoc.; Med. Rec., June 22, 1918).

In 3 cases of **intestinal paresis** following operations for **ovarian cyst** and **ectopic gestation**, quite prompt relief was obtained by injections of pituitary extract. In a case of **subinvolution of the uterus**, the patient suffering from menorrhagia, for which she had recently been curetted without result, and having soft, flabby tissues and low blood-pressure, Aarons decided to try the effect of repeated doses of pituitary extract. Six injections were given in as many weeks. The uterus underwent contraction from 5 to 3 inches as measured by the sound; the general condition was much improved, and had remained so six months after the treatment. During the administration of the pituitary extract marked polyuria was noted. No deleterious effects resulted. The author suggests, however, that the use of the extract in subinvolution be limited to cases with associated low blood-pressure.

Ott and Scott found infundibulin, *i.e.*, extract of the posterior lobe, to act as a powerful **galactagogue** in the goat. In practice its use has at least given rise to a temporary increase of secretory activity.

The writers found that pituitrin not only increased the quantity of milk secreted, but also that it became rich in fats, although this increase is only temporary. The increase in quantity is not so marked, however, after sub-

sequent doses. Hill and Simpson (Amer. Jour. of Physiol., Oct., 1914).

Pituitrin was found to increase muscular activity, leading to constriction of the milk ducts and alveoli of the active mammary gland, with a consequent expression of milk. This action prevailed also on the excised gland in the absence of any circulation. The flow of milk produced by pituitrin is dependent on the amount of milk present in the gland. There is no evidence of any true secretory action. The non-lactating gland, up to a late stage of pregnancy, is not sensitive to pituitrin. Gaines (Amer. Jour. of Physiol., Aug. 1, 1915).

As a galactagogue the writer employs pituitary extract by mouth with as great confidence as he does ergot to cause uterine contraction after labor. He has noted no unpleasant phenomena from it. Its action proved permanent. H. C. Hughes (Therap. Gaz., May, 1915).

Infectious Diseases.—In this general class of disorders the use of pituitary acts, from my viewpoint, and in keeping with the effects of adrenal preparations, by enhancing the immunizing activity of the blood and the tone of the cardiovascular system. That such was the case in the infectious diseases in which it was tried can only, however, be surmised.

Adrenalin and pituitrin were used in combination in cases of marked circulatory disturbances characterized by depression in children in **pneumonia, diphtheria,** and **typhoid.** He injected 0.25 c.c. (4 minims) of a 1:1000 pituitrin preparation and 0.5 c.c. (8 minims) of a 1:1000 adrenalin solution in young children, and double the dose in older children, repeated every 6 hours, about the duration of the rise of blood-pressure. In the interval camphor or caffeine was injected. P. Rohmer (Münch. med. Woch., June 16, 1914).

The writer studied the effects of pituitary injections on blood-pressure of febrile patients in 15 cases, 6 of whom had pulmonary tuberculosis, 3 infectious sore throat, 1 exophthalmic goiter, 3 lobar pneumonia, 1 surgical shock, and 1 convalescing from typhoid. From 1 to 1.5 c.c. (16 to 24 minims) of extract of pituitary gland was injected deep into the muscle of the arm. The blood-pressures were taken several times before the injection, and thereafter at intervals of about 15 minutes for 1 hour or more. The pulse rate, temperature and rate of respiration were also noted. Aside from an occasional slowing of the pulse rate, which never exceeded 10 beats per minute, no definite change in these occurred. The rise in the diastolic pressure amounted in some instances to 15 mm. Hg. or more, and this, together with its time and relative constancy, made it certain that it was due to the action of the drug. Schmidt (Arch. Internal Med., June, 1917).

Rénon and Delille found that in **typhoid fever** it raised the blood-pressure, slowed the pulse, increased diuresis, and improved the patients in general, hastening convalescence noticeably. In **diphtheria,** in which the toxin reduces the vascular tension and promotes cardiac complications, it lowered the pulse rate, raised the blood-pressure, and increased diuresis. In **erysipelas** it seemed to hasten the favorable evolution of the disease. In **pneumonia** it raised the blood-pressure when this became low, but without influencing favorably the evolution of the disease. In **bronchopneumonia,** however, the opposite proved to be the case, considerable benefit being noted. **Influenza** was found to be very favorably influenced, rapid recovery resulting in patients aged, respectively, 80 and 63 years. This was confirmed by Azam, in the infectious form. Rénon and Azam enumerate the phenomena which, in in-

fectious diseases, indicate the need of pituitary: 1, a fall of the arterial tension; 2, quickening of the pulse and, as complementary minor phenomena, insomnia, anorexia, abnormal sweating, and heat flushes. Under the influence of pituitary there occur: 1, increase of arterial tension; 2, slowing of the pulse, with increase of power and amplitude; 3, increased diuresis; 4, increase in weight; 5, hastening of convalescence.

In several cases of tuberculosis treated by Rénon and Delille, the results were not, on the whole, encouraging. In a case of **Addison's disease** complicating tuberculosis, however, there was a notable rise of the blood-pressure and diminution of the asthenia. Trerotoli had already noted the beneficial effects of pituitary body in **Addison's disease**—a fact which further suggests that the active agent of pituitary substance is its adrenal component.

Exophthalmic Goiter.—Rénon and Delille obtained considerable improvement in this disease by the use of pituitary gland. From the fourth to the fifth day, the sleeplessness, tremor, digestive disturbance, sweating, and sensation of heat were considerably lessened. The tachycardia improved less rapidly, the pulse becoming slower gradually and attaining its slowest rate toward the fifteenth day. The arterial tension also rose steadily, attaining the maximum toward the third week, falling again somewhat, but not to the former low level. Some diminution of the exophthalmus occurred, but the goiter was not reduced. The dose administered was 4½ grains (0.30 Gm.) of the whole pituitary (ox) gland daily, a dose which they deem advisable to increase to 7½ grains (0.50 Gm.) in divided doses daily. The symptoms tend

to return, however, on discontinuing the remedy. Cases subsequently treated were also benefited, but no cures were effected. It is well to remember in this connection that the dose of the dried pituitary available in this country is but 2 grains.

This mode of action, from my viewpoint, corresponds precisely with that referred to under the preceding heading. We have seen that the main pathological condition—that to which all the prominent symptoms of exophthalmic goiter were due—was a general dilatation of the arterioles. Pituitary extract causing constriction of these vessels as long as it is administered, it offsets for the time the morbid phenomena enumerated. That such is actually the case was demonstrated by Hallion and Carrion, who found, experimentally, that pituitary extracts "always produced their effects by raising the arterial tension," producing at the same time "an intense vasoconstrictor action upon the thyroid body." Briefly, we have here precisely the physiological action necessary, the vasoconstrictor power of the adrenal component of the pituitary gland superseding the vasodilator action of the thyroid, the underlying cause of the disease.

Nervous and Mental Diseases and Myopathies.—Rénon and Delille used pituitary in 10 **neurasthenics** in whom tachycardia; irregular vascular tension, often below normal; a sensation of oppression, myasthenia, insomnia, and anorexia were present. In these cases 3 to 5 grains (0.2 to 0.3 Gm.) daily proved remarkably useful, though no complete recovery was noted. This dose refers only of course to the whole gland.

Delille and Vincent obtained a com-

plete recovery in a grave case of **bulbospinal myasthenia** by the simultaneous use of pituitary and ovarian extracts. Parhon and Urechia and Léopold-Lévi and de Rothschild had also obtained favorable results with pituitary in similar cases. Browning observed good effects in cases of **chorea** in which this disorder occurred in conjunction with **stunted growth,** as shown under the next heading.

In epilepsy it was tried by Mairet and Bose, but only served to increase the number of attacks—a result to be expected, since Spitska has shown that these were due to abnormal elevation of the blood-pressure. In some instances it provoked delirium.

Sollier and Chartier tried pituitary in **mental disorders** and found it useful in depressive states. It raised the blood-pressure, reduced the pulse, suppressed profuse sweating, and improved the asthenia. The synthesis of perceptions and the association of ideas were improved, and mental operations were incited more promptly.

Stunted Growth and Imbecility.— In a case in which a child of 3 years had shown the evidences of **hypothyroidia** with **idiocy** sufficiently to suggest the use of thyroid, Léopold-Lévi and de Rothschild found this agent useless. The case being attended with marked **myasthenia**, they administered pituitary extract, 1½ grains (0.1 Gm.) twice daily, which corresponded with 7½ grains (0.5 Gm.) of the fresh gland. Marked signs of improvement appeared within a few days. The intelligence developed to a remarkable degree, and soon reached that of a child of a corresponding age, 3 years, though before the treatment it did not exceed that of a 7 or 8 months' infant. Two similar cases,

one of which showed symptoms of Little's disease, were similarly benefited.

Browning used pituitary only in **undersized** or **backward children and youths** (not real dwarfs or midgets), and obtained results both as height and weight in 4 cases described. The newly discovered tethelin is thought to have special properties in this direction.

> The daily addition of 50 to 75 Gm. (1⅔ to 2½ ounces) of fresh desiccated defatted anterior lobe of the ox to young dogs failed, except in some instances, to stimulate their growth as evidenced by their weight. Nor was their growth impeded. In white rats (Amer. Jour. of Physiol., Nov., 1912) the same investigator noted the inability of anterior lobe to stimulate growth. In fact, it seemed to impede growth. T. B. Aldrich (Research Lab. P., D. & Co., vol. i, 1913).
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> The writers, in experiments in animals, the gland being given in sufficient amounts to represent the relative weight of an average man, found that "neither anterior nor posterior lobes had any effect on the weight or growth of the animal." Lewis and Miller (Arch. of Med., Aug. 15, 1913).
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> The growth of young fowl was retarded by the addition to the diet of fresh, unmodified anterior lobe of ox pituitary, as shown both in body-weight and in length of the long bones. Involution of the thymus accompanied this retardation and may have borne a causal relation to it. These effects are more marked in the males than in the females. R. Wulzen (Amer. Jour. of Physiol., May, 1914).
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> A striking fact in the therapy of *cretinism* is that symptoms due to hypothyroidism clear up under pituitary gland. In a personal case there was a striking change in the contour of the hands, ankles, hips, buttocks, thighs and shoulders that could be made to appear or recede by giving or taking away pituitary gland. The

effect on the child's disposition was also striking. R. S. Haynes (Jour. Amer. Med. Assoc., June 19, 1915).

The effect of giving 4 mg. (1/16 grain) of tethelin per day by mouth to mice for from 5 weeks onward, was found by the writer to be similar to that of pituitary tissue, viz., initial retardation of growth, followed by acceleration. Both effects were so exaggerated, however, as to involve total distortion of the curve of growth, the second growth-cycle being enormously prolonged, the third abbreviated and accelerated. T. B. Robertson (Endocrinology, Jan., 1917).

Intestinal Paresis.—Bell and Hicks have found pituitary extract of value in paralytic distention of the intestines. It never failed either in postoperative or other paresis if given intramuscularly when the intestine begins to distend in 15-minim doses (0.92 c.c.), repeated in an hour if required. The effect is then sustained by daily doses if need be. The beneficial influence of the injections was, as a rule, noticeable in a few minutes.

Twenty-one cases illustrating the fact that pituitary extract has a very marked effect upon the muscular coats of the bowel, and that it is able to overcome the **temporary paralysis due to exposure after abdominal operations.** This is shown by the early passage of flatus and by the absence of abdominal discomfort. In only 3 cases did the bowels act without the assistance of the enema, but in every case except 2 a satisfactory action of the bowels was obtained after a simple enema, and it was unnecessary to give any aperient by the mouth. L. A. Bidwell (Clinical Journal, Sept. 6, 1911).

In **postoperative cases,** often as a routine procedure, the writer found pituitrin very beneficial in starting intestinal activity as an aid to enemata or drugs given by mouth; repeated hypodermic injections often overcame symptoms simulating **intestinal paresis.** S. W. Bandler (Med. Rec., Feb. 12, 1916).

Good results were obtained by the writer from pituitary extract in the cases of **intestinal paralysis** frequently **following operations** for acute appendicitis with general peritonitis. In some of these intestinal paralysis is the only manifestation of the peritoneal inflammation, and at times the patient's life might be saved if the paralysis were overcome. In a case of gangrenous appendicitis in a child of 10 years, with marked abdominal distention and absence of bowel movements for 6 days after the operation in spite of gastric lavage, enemas, and castor oil suppositories, a first subcutaneous injection of 1 c.c. (16 minims) of pituitary extract (posterior lobe) brought colicky pains and a small stool within 15 minutes. Further injections on subsequent days were promptly followed by increasingly copious bowel movements, and recovery took place. In another case, that of a soldier suffering from intestinal occlusion, whose bowels had not moved 16 days, equally good results were obtained. E. Kirmisson (Bull. de l'Acad. de méd., Jan. 29, 1918).

To prevent postoperative nausea, vomiting, and gas pains following abdominal operations the writers recommend pituitrin hypodermically. The method used is as follows: Morphine, 1/6 grain (0.01 Gm.) and atropine, 1/180 grain (0.00035 Gm.), hypodermically 1 hour before operation. Immediately after operation they give 1 c.c. (16 minims) of pituitrin hypodermically. This same dose is repeated in 2 hours. Two hours later, 1/2 c.c. (8 minims), and 4 hours later another 1/2 c.c. (8 minims). Where too much handling of the viscera has not occurred, no more pituitrin is given, but in severe operations, doses of 1/2 c.c. (8 minims) are continued every 4 hours for 24 hours. They give 3 grains (0.2 Gm.) of calomel in 1/2-grain (0.032 Gm.) doses every 1/2 hour, followed by a saline cathartic.

On the basis of 126 cases, of which 104 were non-septic, 22 septic, and 9 cases of **eclampsia,** the writers conclude as follows: (1) Pituitrin is a valuable drug in stimulating the muscular coat of the intestine after abdominal section in non-septic cases. (2) It is of decided aid in preventing postoperative shock in non-septic cases of abdominal section, as evidenced by lack of rise of temperature or pulse-rate. (3) It does not appear to have any influence in cases complicated with septic peritonitis. (4) It stimulates the secretory activity of the kidneys in eclampsia. (5) It materially reduces the postoperative suffering. Davis and Owens (New Orleans Med. and Surg. Jour., lxx, 712, 1918).

Pituitary gland is also of value in the intestinal paresis following pelvic operations.

ORCHITIC OR TESTICULAR ORGANOTHERAPY; SPERMIN.

The mode of action of these agents has not as yet been explained otherwise than by the process I have suggested, viz., that it is similar to that of the adrenal products, owing to the presence in these preparations of the adrenal principle.

That the testicle influences powerfully the organism at large is well shown by the fact that castration before puberty modifies in many particulars the development of the individual. They preserve to a certain extent the characteristics of infantilism, the skin remaining soft and white, their muscles flabby and weak, and the voice highpitched. Yet they are usually tall, owing to inordinate growth of the bones. They lack courage, initiative, and intelligence. It is evident, therefore, that the testicles do not solely carry on genital functions. Brown-Séquard, in fact, taught that they carried on a dual rôle:

1, procreation; 2, the production of an internal secretion which stimulates and sustains the energy of the nerve-centers and cord, and capable, moreover, of endowing the individual with physical, moral, and intellectual characteristics of sex. His own physical and intellectual activity having been greatly improved at the age of 72 years, by injections of an extract prepared from the testes of young dogs, he concluded that it possessed marked therapeutic value. No one who, as I did, saw Brown-Séquard before and after he had submitted himself to this treatment could stretch his imagination sufficiently to attribute the change in his appearance to autosuggestion. He literally looked twenty years younger. Unfortunately, the value of testicular preparations was exaggerated by many observers to such a degree that their use fell into disrepute, and the subject has received but little attention in recent years.

The prevailing opinion at the present time is that the beneficial effects obtained from testicular preparations are not due necessarily to an internal secretion, though the existence of such is not denied, but to nucleoalbumins, substances that are rich in phosphorus, resembling greatly lecithins and glycerophosphates.

In a eunuchoid studied by the writer the height was below the average in relation to body weight, while lymphocytosis was insufficient. But there was no change in the sympathetic or autonomous excitability; the conditions of metabolism were normal; there was no disturbance of oxidation; no alimentary glycosuria nor hydruria. E. Voelckel (Berl. klin. Woch., Apr. 15, 1918).

A personal analytic study of the question brought out a suggestive

fact, viz., that "spermin," which may be obtained not only from testicles, but from the ovaries of mammals and fish roes, presents the characteristics of the adrenal secretion, both as to composition and physiological action. As I pointed out in 1903 (see "Adrenal Extract," *supra*), the adrenal secretion serves to take up the oxygen of the air and carry it to all parts of the body as the active constituent of hemoglobin. As such it sustains oxidation and metabolism. Now, Batty Shaw ("Organotherapy," 1st ed., p. 205, 1905) writes: "Spermin possesses the very curious property of being an oxygen carrier, and, according to Poehl, is responsible for those internal oxidations which take place in the body-tissues. Again, I have urged that the adrenal secretion carries on its oxygenizing function catalytically as a ferment. Pantchenko (reprint from Trib. médicale, 1896) states that "spermin acts catalytically, thus increasing the oxidizing power of the blood, and simultaneously activates the intraorganic oxidation processes where these are weakened." Moreover, as is the case with the active adrenal secretion, spermin gives the guaiac and Florence hemin test (Mari); it is, as a constituent of orchitic extract, unaltered by boiling (Dixon); it increases the force and regularity of the heart much as does digitalis (McCarthy); it enhances the resistance to disease; it increases the production of urea; it acts directly upon the cardiovascular system. Moreover, as shown by Poehl—a fact which indicates that it is not specific to the testis—it is a ubiquitous constituent of the whole organism, in the female as well as the male.

Poehl having found in 1895 (Zeit. f.

klin. Med., Bd. xxvi, H. 1 u. 2) that spermin was present in all the different parts of the organism, it becomes a question whether its actual source is the testicle, as believed by him, or whether, as I hold, it is derived from the adrenals, the testicles being richly supplied with it only because of the importance of their functions, *i.e.*, procreation. The relative importance of both sets of organs to life answers this question. If, as Poehl says, "it is the oxidizing action of spermin which plays the principal rôle in the phenomena it produces," the organs whose removal arrests oxidation sufficiently to render life impossible must be the source of the oxidizing agent. As is well known, removal of the testicles does not kill, while death invariably follows extirpation of both adrenals. It is plain, therefore, that the testicles do not produce the oxidizing substance shown by Poehl and others to be the active agent in spermin, and that it is the oxygen-laden adrenal secretion (adrenoxidase) it contains which endows it with therapeutic properties.

On the whole, the foregoing facts have shown that, while, as held by Dixon, orchitic extract is a compound of phosphorus-laden bodies, nucleins, lecithin, etc., which acts much as do glycerophosphates and similar products (though containing spermin in relatively small quantities), spermin owes its beneficial effects to the fact that it is rich in oxygenized adrenal secretion, *i.e.*, the product I have termed adrenoxidase.

After much experimentation at the Collège de France, the writers were able to cause healing of extensive and deep **wounds** in a few days, by applying locally the pulp of sex glands procured by castrating young animals. The cells of these glands,

through the secretion they contain and which is absorbed by the wound, exert an intense accelerating action on the process of granulation. The organ found most effectual in these experiments would, *a priori,* have been considered that most suitable, owing to its especial vital energy. Animals deprived of these organs are known to accumulate fat at the expense of their muscles and to become apathetic and passive. In the wounds treated with this material, its use often had to be discontinued after a few days in order not to exceed the results sought and cause projection of new tissue beyond the level of the wound cavity by reason of a too intense development of granulations. With the aid of this treatment its sponsors hope to spare the wounded long months of suffering and considerably shorten their stay in hospitals. Voronoff and Bostwick (Presse méd., Sept. 9, 1918).

THERAPEUTICS.—The fact that testicular preparations, including spermin, have been recommended in a large number of disorders has not served to recommend them to the impartial observer. The use of orchitic extract was extolled in various nervous disorders, especially **tabes, neurasthenia, melancholia, impotence,** and **paralysis agitans**; in several cutaneous disorders, **eczema** and **psoriasis**; in disorders of nutrition, **gout, obesity,** and **glycosuria**; but others again have failed to obtain any favorable results. Spermin has also been recommended by Poehl and his followers not only in the majority of the foregoing disorders, but in many others besides, in **acne, rheumatism, syphilis, marasmus,** and in various infections, such as **typhoid fever, diphtheria,** and even **cholera.** It has been tried in **Addison's disease,** but adrenal preparations are to be preferred.

Emulsions of sex glands are available sources of material for hormone therapy. The essential sex hormone is a powerful physiological cell stimulant and nutrient. The writer recommends it for the treatment of early stages of **arteriosclerosis,** nutritional diseases and certain functional neuroses. Lydston (Jour. Amer. Med. Assoc., May 13, 1916).

In the light of the analysis submitted above, however, there is good ground for the belief that beneficial effects were obtained in all these maladies. That the nucleoalbumins of orchitic extract, acting as would glycerophosphates, could be beneficial in the disorders enumerated, no one can deny. This can hardly be said, however, of the cutaneous and nutritional disorders, unless the spermin the extract contains, by enhancing oxidation and the destruction of toxic wastes, proves to be the active agent. Spermin itself—as adrenoxidase—is unquestionably capable of doing this actively, and in **syphilis** and **marasmus** of markedly enhancing the functional activity of all tissues. Again, the beneficial rôle of spermin in **infections** finds its explanation in a fact I have repeatedly emphasized, viz., that the oxygenized adrenal secretion, the active agent of spermin from my viewpoint, is an active participant in all immunizing processes, local and general.

The main point to determine, however, is whether orchitic extract or spermin affords better or as good results in any of the disorders enumerated than other remedies at our disposal. The evidence available indicates that such is not the case. Hence, the disuse into which the testicular products have fallen.

OVARIAN ORGANOTHERAPY. —The ovaries correspond in many

ways with the testes in their influence upon general development: their removal in children causes them to grow up without feminine attributes; absence of these organs prevents development of the uterus and the appearance of menstruation; their removal after puberty arrests menstruation and leads to atrophy of the genital organs. These phenomena were attributed by Curatulo, in accord with Brown-Séquard's doctrine, to the loss of what influence an internal secretion supplied by the ovaries to the body at large possessed over its development. The administration of ovarian substance in subjects deprived of their ovaries or during the menopause produced a marked amelioration of all distressing phenomena.

> The ovarian internal secretion being elaborated by the interstitial cells the latter probably correspond to the lutein cells of the theca interna of the atresic follicle. The interstitial cells of the ovary are analogous to the testicular interstitial cells of Leydig, known to elaborate an internal secretion. Hence ovarian therapy should include at least the product of the interstitial cells. Extracts of ovaries of pregnant animals, with exclusion of the corpora lutea, proved superior therapeutically to extracts of whole ovaries of non-pregnant animals which included the corpus luteum. W. P. Graves (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 30, 1917).

The manner in which ovarian extract produces its effects has remained obscure. As Wilcox ("Pharmacology and Therapeutics," 7th ed., p. 824, 1907) says: "But little is known of its pharmacological action. Fresh ovarian extract is said, when injected into the circulation in rabbits, to raise the blood-pressure, diminish the heart's action, and slow the respiration, and when administered to the human female also to increase the arterial tension. In the castrated animal it is found to increase oxidation to somewhat above the normal degree, but on the normal animal it has no such effect." These are the identical effects produced by adrenal preparations. From my viewpoint, it is, in fact, owing to the presence of this substance—not necessarily an internal secretion—in the ovaries that they must be attributed. There exists, as shown by Schäfer, a close homology between the interstitial of the ovary and the same cells in the adrenals; both sets of organs are derived from the Wolffian body; ovarian extract raises the blood-pressure and slows the heart, as shown by Federoff, Jacobs, and others. Removal of the ovaries, moreover, reduces the oxygen intake 10 per cent., as shown by Loewy and Richter, while ovarian extract restores it; it has been, therefore, regarded as an oxidizing ferment. Neumann and Vas noted that ovarian extract enhanced metabolism; Senator observed that ovarian preparations increased diuresis and the excretion of urea and phosphoric acid. Its physiological effects are those of adrenal preparations, therefore, in every respect.

Its effects on oxidation are so striking, in fact, that they have been clearly recognized by many clinicians. "We are authorized to classify ovarian organotherapy among the oxidizing agents," write Dalché and Lépinois. "This conclusion, it must be admitted, is that reached by several authors. Curatello and Tarulli believe that the internal secretion of the ovaries favors the oxidation of phosphorized organic substances, hydrocarbons, and fats. According to Gomes, it enhances oxidation and hydrolysis and favors the elimination of phosphates. . . .

Albert Robin and Maurice Binet have shown that there is during menstruation an increase of the respiratory exchanges. Keller, studying the general exchanges, found that there was increased nitrogen oxidation. We have ourselves found that menstruation, in itself, enhances vital functions and particularly the great function of general oxidation." Mathes noted a reduction in the excretion of the phosphates, in women whose ovaries had been removed

> The ovary appears to preside in some way over the metabolism of inorganic matter, and, hence, aids in maintaining the composition of the blood. Thus when young bitches are castrated there is an initial reduction of the number of erythrocytes and amount of hemoglobin. Offergeld (Deut. med. Woch., June 22, 29, 1911).

> The investigations of the writers sustained Loewy and Richter so far as the reduction in metabolism after castration is concerned. Removal of the ovaries of dogs caused an increase in weight by lowering metabolism in one from 12 to 17 per cent., and in the other from 6 to 14 per cent. Murlin and Bailey (Trans. Amer. Gynec. Soc.; N. Y. Med. Jour., Aug. 11, 1917).

PREPARATIONS AND DOSES.
—The preparation in general use is the *desiccated gland*, available in the form of 2-grain tablets, which may be given in doses of 2 to 4 grains (0.132 to 0.26 Gm.) twice daily. The *fresh organ* may be employed in 10- to 15- grain (0.6 to 1.0 Gm.) doses where the pharmaceutical product is not available. As the patient becomes readily habituated to the remedy, it is best to begin with small doses and to increase them gradually. It owes its action to the corpus luteum it contains.

THERAPEUTICS.—As in the case
of testicular preparations and spermin,

ovarian extractives have been tried in a multitude of disorders with more or less benefit or without any whatever.

Natural and Artificial Menopause. —In disorders occurring in the course of the **physiological menopause,** or when the latter is produced by bilateral oöphorectomy, ovarian preparations have proven of considerable value in a large proportion of cases since Brown-Séquard first introduced their use. Experience has shown, however, that the improvement lasts only as long as the agent is administered, and that, furthermore, certain phenomena: the palpitation, trembling, and "nervousness," disappear earlier than the others, *i.e.*, the asthenia, flushes, irritability, and psychoses, though effects in all symptoms, including the cutaneous disorders—especially acne rosacea and eczema—are promptly realized, sometimes as early as the fourth day.

These effects are normally explained by the influence of the remedy on general oxidation and the improvement of the antitoxic functions of the blood, the imperfect hydrolysis of tissue wastes being the underlying cause of the phenomena other than the general asthenia.

The best results are obtained in young women who have grown obese after removal of the ovaries, or in whom **obesity** is due to ovarian insufficiency. In physiological menopause they are less marked, as a rule, and sometimes fail altogether to appear. In such instances, good results may sometimes be obtained by giving simultaneously 1 grain (0.066 Gm.) desiccated thyroid, or by depending upon the latter remedy alone. In the **amenorrhea** of congenital ovarian insufficiency, desiccated ovary has caused the appearance of menstruation.

W. E. Dixon, of Cambridge Univer-

sity, recalls that the presence of ovarian tissue in the body, however small in amount, is sufficient to prevent the distressing symptoms which frequently follow complete extirpation; even transplanted ovaries are sometimes able to prevent the menopause attending removal of the ovaries. Hence, the beneficial effects of ovarian preparations.

Improvement has also been obtained by some observers in **acne, prurigo,** and **eczema.** They have been found to cause an increase of the red corpuscles in **chlorosis** and to afford benefit in **gout, epilepsy, exophthalmic goiter** and **obesity,** and also in **dysmenorrhea.**

> One must give an active preparation in dosage sufficient for results, *i.e.,* until the symptoms disappear. He had good results combating **high blood-pressure** at the climacteric, and **arteriosclerosis** may be thus prevented. All cases with hypofunction of the ovary are indications, especially **amenorrhea** and so-called **lactation atrophy.** In dysmenorrhea it is indicated if all other measures fail; likewise in **hyperemesis,** psychoses, especially **dementia precox, postpuerperal depression** and **hyperexcitability.** C. B. Bucura (Jahrb. f. Psychiat. u. Neurol., xxxvi, 1916).
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> In 2 cases of **kraurosis vulvæ,** permanent relief was obtained in 1 with ovarian extract; the other was temporarily improved after injecting the latter. The sole criterion was a change from the dry glistening unyielding tissue to a soft, moist, and pinkish mucosa, which bore no evidence of scratching. G. Gellhorn (Trans. Amer. Gynec. Soc.; N. Y. Med. Jour., Aug. 11, 1917).

Of late, the general attention has been centered upon the therapeutic use of the essential structure of the ovary, the corpus luteum, although Graves and others have emphasized also the importance of the interstitial cells.

CORPUS LUTEUM ORGANO-THERAPY.

The consensus of opinion up to now has been that the internal secretion of the ovary is produced by the corpus luteum. The function of the corpora lutea in the early stages of their life is to initiate growth processes in the uterine cavity by means of this internal secretion and subsequently to preside over the nidation and development of the ovum, and the cyclic engorgement preceding menstruation. The labors of Fraenkel confirming his previous investigations have strongly sustained the internal secretion theory and its controlling influence over the above functions.

> The 2 most important prerequisites to success in the use of this drug are: 1. The selection of a preparation made exclusively from the corpora lutea of pregnant animals, and, 2, due attention to the fact that the action of the drug is frequently slow in asserting itself, and that the drug should be given up only when thorough trial has demonstrated its lack of efficiency. L. T. de M. Sajous (N. Y. Med. Jour., Jan. 29, 1916).
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> The relationship between character and degree of lutein structure to the disorders of menstruation, such as metrorrhagia and menorrhagia, was recently studied by the writer in 137 cases. The corpus luteum, he says, should be studied from the standpoint of origin in the lutein cells. Cases of amenorrhea show characteristically corpora lutea. It is absent in young girls and in the fetus, also in the menopause. With amenorrhea of lactation it is present, the functioning breast probably presenting an inhibiting secretion. In metrorrhagia and menorrhagia there were negative findings and no histological changes could be found connected with menstrual disturbances. The theca interna instead of advancing from lutein cells simply regresses. The

granulosa cells are formed before the lutein cells, and the latter are formed from them. The internal secretion goes back into the blood. Hence the vascularization. E. Novak (Med. Rec., June 17, 1916).

Summarizing the labors of Fraenkel, Loeb, and Novak, the writer concludes that the corpus luteum makes possible the formation of maternal placenta by supplying a sensitizing substance to the uterine mucosa. Fixation of the embryo is aided by the activity of the corpora lutea. The corpus luteum is apparently essential for the development of the embryo early in pregnancy. The presence of corpora lutea militates against ovulation, i.e., lengthens the sexual cycle, at least in the guinea-pig. The presence or absence of corpora lutea means presence or absence of menstruation, and possibly their hypo- or hyper- function means, in part at least, dysmenorrhea or menorrhagia. The activity of lutean secretion affects development of the mammary gland, even to free secretion of milk. E. T. Hermann (Minn. Med., May, 1918).

As to the manner in which the sensitizing substance referred produces its effects, it is not explained. From my viewpoint they are the result of the presence in the corpus luteum of an energizing principle similar to the adrenal active principle in organic combination with highly specialized specific nucleins.

PREPARATIONS AND DOSES.—The preparations available include desiccated corpus luteum (*glandulæ luteæ desiccatæ*), which may be given in 5- to 10- grain (0.3 to 0.6 Gm.) doses three times daily. It is usually administered before meals, but if, as is sometimes the case, it causes gastric disturbances it may be administered during, that is to say, in the course of, the meal. The term "lutein"

is sometimes applied to the same product, but it is misleading, and its use should be discouraged.

Considerable personal experience showed that corpus luteum should be given in sufficient doses, and over a long period of time to accomplish satisfactory results. It produces no toxic effect except a feeling of fullness in the head or vertigo, and its action is not cumulative. H. E. Happel (Med. Rec., May 19, 1917).

A liquid preparation of corpus luteum extract is also available, 1 c.c. (16 minims) of which represents 20 milligrams (⅓ grain) of the dried substance.

THERAPEUTICS.— The indications for desiccated luteum are similar to those for ovarian preparations.

It is generally regarded as superior to them, however, particularly for the nervous phenomena of **menopause,** natural as well as operative, **irregular** or **scanty menstruation** particularly if accompanied by neurasthenia, **dysmenorrhea, sexual anesthesia, pruritus vulvæ** and **infantile uterus.**

The writer uses an extract derived from the ovaries of pregnant animals. He gives 5-grain doses (0.3 Gm.) 3 times every day. The blood-pressure of the patient should not be allowed to fall more than 15 mm. below the patient's normal pressure, and never below 90 mm. The particular conditions for which the drug is found serviceable are: **Functional amenorrhea** or **scanty menstruation;** **dysmenorrhea of ovarian origin;** manifestations of physiologic or **artificial menopause,** such as nervous or congestive disturbances of reflex origin (**hot flushes, psychoneuroses,** etc.), "neurasthenic" symptoms during menstrual life; **sterility,** not due to pyogenic infections or mechanical obstructions; where the function of 1 ovary is impaired, or 1 ovary has been removed, and the compensatory

activity of the other is insufficient; repeated abortions, not due to disease or mechanical factors, and **hyper-emesis in early pregnancy.** W. T. Dannreuther (Jour. Amer. Med. Assoc., Jan. 31, 1914).

Autotransplantation of the corpus luteum was resorted to by the writer in 2 cases. Both women complained of nausea and vomiting for several days after operation. In neither case was the implanted body palpable in the broad ligament at a later operation. DeLee (Surg., Gynec. and Obstet., Jan., 1916).

In menstrual epistaxis all styptic agents, even in local application, are contraindicated; the medication of choice should be physiological; that is to say, the secretions of the corpus luteum. The writer gives hypodermic injections of this substance and this treatment has generally been found sufficient for controlling even the most severe types of **menstrual epistaxis.** Bab (Münch. med. Woch., Nov. 13, 1917).

Menopause symptoms of ovarian extirpation are largely ameliorated by ovarian extract. Its symptoms are vasomotor disturbances, hot flashes, head flushings, indigestion (perhaps due also to circulatory disturbance), the addition of weight mostly in the form of fat, sometimes nervous irritability, sleeplessness or the reverse, *i.e.,* unusual daytime drowsiness and mental sluggishness. How many of these symptoms are due to loss of ovarian secretion, or to the sudden cessation of menstruation without pregnancy and consequently a storing in the system without physiological need of the nutriments and salts of the blood which were previously lost, has not been determined, but both are factors in the condition. The normal menopause or the cessation of menstruation without pregnancy at a younger age will cause more or less symptoms and ovarian feeding may markedly improve the condition.

The writer considers the use of ovarian extracts in the following conditions: (1) after extirpation of the ovaries; (2) for menopause symptoms, especially when the onset is abrupt; (3) for too slowly developing girls; (4) when there is an apparent subsecretion of the ovaries in older girls and women, especially when a long course of treatment is necessary; (5) in menstrual disturbances. He discusses the results obtained. He also records his results in the use of corpus luteum in: (1) amenorrhea; (2) overweight; (3) dysmenorrhea; (4) pregnancy; (5) menopause cases.

It is unimportant whether it is the ovarian substance or the corpus luteum that furnishes the secretion that is most necessary for the mature woman's mental and physical health; it is a fact that many internal secreting glands are disturbed by the removal of the ovaries. Total removal of the ovarian tissue before puberty stops the development of the genital organs and of the breasts. Total removal after puberty stops menstruation, causes artificial menopause, and multiplies the menopause symptoms and disturbances. The younger the adult woman so castrated, the more serious are the symptoms. Castrated women are often left in a serious mental and physical condition. Feeding these sufferers ovarian and corpus luteum extracts is only partially successful in ameliorating their condition.

The rules for operation for tubal and ovarian disease should be: 1. As much of the ovaries as are found healthy should be left. 2. If the operation of necessity destroys the circulation and therefore nutrition of the whole of both ovaries, large grafts from the healthy part of the ovaries should be placed in some location that will allow the ovarian tissue to readily obtain a blood supply and therefore live. If the ovarian transplant lives and functions, it should be remembered that it periodically swells, and hence, in tense, nondilatable tissue, may cause severe pain. The uterine wall, the peri-

toneum, the labia majora, the mons veneris, the abdominal wall, and even the axilla have all been suggested as regions for implantation.

If there is no healthy ovarian tissue for autografting, since total extirpation of both diseased ovaries is not an emergency operation, the surgeon connected with a large hospital generally could obtain a piece of healthy ovary from a non-syphilitic and non-tuberculous patient for transplantation into the woman to be castrated. The necessity for obtaining such ovarian tissue would be rare, as total extirpation is rarely needed. Of course the surgeon cannot decide that there is no healthy ovarian tissue until the time of the operation, but he should be prepared for such an emergency when there is a probability of the necessity of total extirpation. Ovaries removed from healthy women after sudden accidental death, and properly preserved, would seem to be ideal tissue.

If these engrafted ovaries or ovarian tissues live and function, it may be 2 or 3 months before the fact is known by any symptoms or signs in the patient. The signs of success are a general feeling of health, absence or diminution of menopause symptoms, and menstruation. Such grafts may live for a time and then die, but more or less embryonic ovarian tissue may have had time to mature and to begin to furnish the secretion so much needed by the patient.

Properly selected patients, who have had their ovaries removed for disease and who have psychoses which are not cured by the administration of organic extracts, might well be treated by grafts of healthy human ovarian substance. O. T. Osborne (N. Y. Med. Jour., cviii, 447, 1918).

The writer used the liquid luteum extract hypodermically in 2 cases of **repeated abortion** without demonstrable cause with a successful result in both instances. The liquid extract was given intramuscularly in 1-c.c.

(16 minim) doses, 36 being given the one case over a period of 2 months, and 32 in the second case over a period of 9 weeks. In one the 4 previous pregnancies had never gone beyond 3½ months, while in the first case, the several abortions had recurred about the third month. Such cases are referred to in text-books as "irritable uterus," but the writer tentatively attributes the repeated abortions to untimely absorption of the corpus luteum. J. Cooke Hirst (Amer. Jour. of Obstet., Apr., 1918).

Through the use of corpus luteum there is a tendency in the body to retain nitrogen and put on flesh; it has a marked vasodilator effect; the development of the mammary gland depends upon the formation of corpus luteum; the fixation of the embryo, the formation of the decidua and menstruation depends upon the secretion of the corpus luteum. Extracts of corpus luteum, however, do not replace the function of the normal gland. It is a true puberty gland and an antagonist of the pituitary. Extract of corpus luteum causes diminution of nitrogen excretion in the urine, diminution of oxygen absorption, unstable output of carbon dioxide, increased activity of sweat glands, and a marked fall in blood-pressure. With these physiological data on hand, extract of corpus luteum has been used by clinicians in syndromes believed to be caused by disturbed sexual gland activity. The writer has tried it in the so-called "nervous syndromes" associated with disturbed sexual gland function, and he carefully watched the therapeutic results in a selected number of type cases. Satisfactory results were obtained and, in most instances, very rapidly in menstruation insanity; mild manic depressive insanity; menstruation psychosis; headaches occurring with menstrual disturbance; and symptoms of diminution of hydrochloric acid with menstrual disturbance. There were no results in menstrual disturbance due to obstruction; in menopause due to surgery; cessation

of menstruation with symptoms of acromegaly; in hysteria; or in organic nervous disease. The clinical data following upon these observations were: 1, corpus luteum extract was effective only in the female; 2, it acted best when there was reason to believe the native corpus luteum was still present; 3, the administration of the extract could not replace the function of the native corpus luteum in pregnancy and probably also not in menstruation; 4, when menstruation was discontinued by virtue of disturbance in the secretion of another gland, corpus luteum would not produce menstruation; 5, its action was more or less prompt and small doses were effective; and 6, corpus luteum extract, when effective, produced almost always the same chain of phenomena. H. Climenko (Trans. N. Y. Phys. Assoc.; N. Y. Med. Jour., Feb. 15, 1919).

Corpus luteum has been said to have caused a fall in blood-pressure, it does so in certain cases; in which absence of corpus luteum causes increased pressure. In abnormal cases, those deficient in corpus luteum, corpus luteum extract is helpful. In those cases in which corpus luteum is not the crucial factor, corpus luteum extract does nothing. It is an extension of the principle of nature that one can restore a disturbed cell to normal function more readily than one can put a normal cell into disfunction—the tendency of nature to self repair. Corpus luteum bears a similar relation to blood-pressure as does adrenalin. Whether one gets a rise or a fall of blood-pressure depends on the quantity given. Usually the result is a fall.

One very certain type of individual in whom corpus luteum has given more or less success as a therapeutic agent is a type of girl with certain masculine features; a slight tendency to a mustache, pubic hair growing to the umbilicus, etc. In those cases corpus luteum is almost invariably of service. In administering a glandular product, one is dealing with an enzyme which acts by catalysis, not one which entered into combination with various metabolic processes, but helps metabolic processes along by its mere presence so that in administering it, it is sufficient to give it perhaps at times, only one day in seven, and not necessarily daily. Walter Timme (N. Y. Phys. Assoc.; N. Y. Med. Jour., Feb. 15, 1919).

The reason that the writer did not meet with much success was that he saw the patients 10 to 15 years after operation, and cases neglected to that extent do not respond to corpus luteum. Some do not respond when treatment is administered by the mouth. A. J. Rongy (N. Y. Phys. Assoc.; N. Y. Med. Jour., Feb. 15, 1918).

The writer found corpus luteum tremendously over-rated as regards its value.

In some types of cases he gives corpus luteum to do the opposite of what others prescribe it for. If the patient complains that for so many days before menstruation she is nervous, restless and irritable, it is an index of what was happening under the stimulus of the ripening follicle of the ovaries. Associated with this is the stimulus to the thyroid and the activity of the pituitary. Dysmenorrhea is much more due to the fact that the pituitary is involved than any action of the ovaries. There is an interglandular upset 13 times a year. Many times there is no indication of this until after the birth of a second child, when glandular exhaustion makes a different individual. The writer terms this interglandular upset "constitutional dysmenorrhea." Whether congenital or acquired it is one of the most important indices of the patient's condition. If every man in the medical profession were to pay attention to that factor, they would get a better idea of endocrines. Nine-tenths of the prescriptions in the next 5 years would contain endocrine extracts. S. W. Bandler (N. Y. Phys. Assoc.; N. Y. Med. Jour., Feb. 15, 1919).

KIDNEY ORGANOTHERAPY.

Brown-Séquard, having removed the kidneys and caused uremia, found that the injection of a glycerin extract of kidney prolonged the life of the animals as compared to those in which the same operation was not followed by the use of the kidney extract. This experiment, which has been repeated by others, forms the basis of the belief that the kidney produces an internal secretion. That such a conclusion may not be warranted is suggested by the fact that the kidneys, along with some of the organs so far reviewed, are also rich in adrenal tissue—the so-called "adrenal rests" from hypernephroma sometimes develops—and that as such they are capable, as an active factor in the immunizing functions of the body, of counteracting temporarily the toxemia or "uremia" brought on by removal of the kidneys. Indeed, the relief afforded is but ephemeral, death being postponed but one or two days in rabbits, in which Bitzou repeated Brown-Séquard's experiments. Dromain and de Pradel Bra had also noticed that injections of kidney extract lessened the fits of epilepsy, another toxemia. Dubois and Renaut have already, in fact, attributed antitoxic power to kidney ex tracts.

That we are again dealing mainly with a manifestation of the adrenal principle is further suggested by its powerful blood-pressure-raising property. Tigerstedt and Bergman found that rennin possessed this power; Bingel and Strauss recently confirmed their observation, and found that its action corresponded with that of adrenal and pituitary extracts, those of other organs causing depressor effects. The use of pressure produced by kidney extract was high, i.e., from 40 to 60 mm.

Hg, and lasted from fifteen to thirty minutes. The authors concluded, moreover, that "the action of rennin, like that of adrenalin, is exerted in the muscles of the peripheral vessels." Its general action, however, is more like that of pituitary body extract, the adrenal principle being doubtless combined organically, as in the pituitary, with bodies which prolong and perhaps control advantageously the action of the former. Like adrenal preparations kidney extract also produces myosis.

Even the oxidizing power I have attributed to the adrenal secretion seems to be reproduced; Batty Shaw, who also finds "very little justification for the existence of an internal secretion" in the kidney, remarks that "possibly nephrin and other renal preparations provide a means of stimulating oxidation in general, the kidney merely sharing in this oxidation"—a very accurate estimate from my viewpoint. Shaw adds, moreover, that "similar good results have been reported as a result of treatment by means of spermin and testicular extract," both of which, as I have shown, also owe, in all probability, their therapeutic effects to the adrenal principle they contain.

THERAPEUTICS AND DOSE.

—The therapeutic application of kidney preparations has received considerable attention, and favorable results have been reported in about one-half of the cases of **chronic nephritis,** or **Bright's disease,** in which it was tried. The mode of action, in the light of the facts submitted above, is mainly an increase of the antitoxic power of the blood and diminution, therefore, of the irritation of renal apparatus. Page and Dardelin, for example, report marked amelioration in 18 cases, using a maceration prepared as follows: A very

fresh kidney from a pig is cut into minute pieces, washed with fresh water to remove the excess of urine, then hashed and pounded into pulp. This pulp is put into 300 Gm. (9 ounces and 5 drams) of fresh water to which the physiological proportion of salt, 7.50 to 1000, has been added. It is then allowed to macerate for three hours, stirred occasionally, and kept in a cool place to avoid fermentation. The red water of the maceration is divided into three parts, to be drunk by the patient during the day. It is more conveniently given, however, in tablet form, as "nephritin," prepared in this country by Reed and Carnrick. Only the active substance of the kidney is used in this preparation, the dose being from 10 to 15 5-grain (0.33 Gm.) tablets daily in divided doses, given between meals.

Kidney preparations have also been used with more or less advantage in **puerperal intoxications** and **epilepsy**, but their field is essentially the various forms of nephritis, and particularly for the prevention of **uremia**. They also tend to increase diuresis and reduce the albumin. As stated above, however, favorable effects are to be expected in about one-half of the cases.

THYMUS ORGANOTHERAPY.

In 1907, I submitted evidence which had led me to suggest that the function of the thymus was to supply an excess of phosphorus in organic combination during the growth of the body, *i.e.*, particularly while the development of the osseous and nervous systems demanded such a reserve. This was sustained by the recognized fact that certain diseases of children and adolescents, especially marasmus, rachitis, and trophic disorders of the brain and nervous system, were due, in part, to the functions of the thymus.

The writer carried out the following experimental work. Young rabbits belonging to the same litter were each trephined on the tibia. Some of the animals were fed on thymus gland, the others serving as control animals. The evolution of the bone trauma in each was controlled by regularly repeated radiographic examinations. The writer concludes that the exhibition of thymus gland hastens regeneration of bone traumata. At a given time in repair the difference consisted in the presence of a smaller bone defect, a normal osseous configuration and a moderate callus, while the control animals offered an inverse condition. K. Glaesner (Berl. med. Woch., Nov. 25, 1918).

While this is only adduced as a working theory—the thymus having been the graveyard of many hypotheses—all that can be said for it is that it seems to account for the clinical results obtained under its use better than any hypothesis so far advanced, besides corresponding with the laboratory findings of its effects.

In sexually immature rabbits, fragments of thymus autotransplanted into the subcutaneous tissue of the abdomen after thymectomy were found to take, grow and survive. This confirms other observers' results that thymus removal hastens sexual maturity, and that utilization of rabbits for breeding hastens involution of the thymus. The writers' experiments apply to the transplanted thymus as well. Marine and Manley (Jour. Labor. and Clin. Med., Oct., 1917).

Whatever be the real function of the thymus, certain it is that its production of an internal secretion has not been proved. The evidence in favor of such a theory is but circumstantial at best and very meager. It is equally difficult to prove that the thymus does not produce a secretion. Hoskins (Endocrinology, July-Sept., 1918).

In the light of my own views the thymus supplies lymphocytes *i.e.*, thymocytes, exceedingly rich in nucleins to the body at large for the purposes indicated, but not an internal secretion.

THERAPEUTICS.— Diseases of the Thyroid.—In simple **goiter** it was first tried by Mikulicz, who obtained sufficiently favorable results in 5 out of 11 cases to render operation unnecessary, at least for the time being. Reinbach considers it probably superior to thyroid because the unpleasant effects of the latter are avoided; for the same reason it is especially suitable when organotherapy has to be used continuously. This view is based on the employment of thymus in a large number of cases in the Breslau clinic. Mikulicz gave from 2½ to 4 drams (10 to 16 Gm.) of the raw sheep thymus on bread three times a week, increasing the dose slightly if required.

In **exophthalmic goiter** it had proven efficacious in the hands of Owen in advanced cases, and also in those of Mande when other remedies had been used fruitlessly. The latter gave 45 grains (3 Gm.) daily to a severe case, which greatly improved, relapsing whenever the treatment was interrupted. S. Solis-Cohen also advocates its use in this disease, having found that it exerted its beneficial influence mainly upon the nervous symptoms of the disease without affecting the exophthalmus. Huston White found that the nervous symptoms were alone improved.

These observations coincide with my own view of the manner in which thymus gland produces its beneficial effects. The excess of thyroiodase produced in exophthalmic goiter causes, we have seen, too rapid oxidation of the phosphorus in organic combination

in the tissues, particularly in those of the nervous system, which are extremely rich in phosphorus. Thymus, supplying phosphorus in organic combination, replaces that lost by the nervous system, thus procuring marked benefit in this one direction. As 5 grains (0.33 Gm.) of the dried thymus are equivalent to 30 grains (2 Gm.) of the fresh gland, this dose can readily be given three times daily.

Rachitis, or Rickets.—The same explanation, *i.e.*, the purveying of phosphorus in organic combination—to the osseous system, in the present connection—accounts for the undoubted benefit thymus has procured in this disorder. Mendel, having used thymus gland in 1½ to 3 drams (6 to 12 Gm.) daily in over 100 cases, obtained marked benefit in a large proportion, but especially in the nervous symptoms, including spasm of the glottis. It had previously been tried by Stoppato, but without marked benefit. In Mendel's cases both fresh and commercial tablets were tried, the cases being subdivided as follows: 1, those which showed prodromal symptoms only; 2, those in which deformity of the osseous system was the chief feature; 3, those marked by spasm of the glottis, and, 4, those in which splenic enlargement was the most important sign. Marked improvement was noted in all after from three to four weeks, and dentition and the closure of the fontanelle proceeded satisfactorily. No untoward symptoms were noted—a marked advantage over thyroid preparations. In a case of **stunted growth**, obviously of osseous origin, in a boy of 14 years, R. Webb Wilcox obtained 9¼ inches growth in three years by the persistent use of 2 grains (0.13 Gm.) thymus night and morning.

The view that these effects are due

to the addition of phosphorus in organic combination to the body is further sustained by the results of experimental observation by Hart and Nordmann, that the thymus had a definite relation to assimilation, and that it took an active part in the resistance of the organism to infection. As my own investigations have shown (see the second volume of "Internal Secretions," page 878), nucleoproteid, in so far as its phosphorus in organic combination is concerned, is an active participant in the immunizing process.

Great relief, particularly from the **pain of cancers,** can be attained by the use of thymus extract, according to Takaki. This line of treatment was originally worked out by Gwyer, who showed that there was marked decrease, or even elimination, of pain. The glands used were received fresh. The fat was removed, and the glandular substance cut up and dried at a low temperature by a forced draught of air, then ground and sifted to a uniform powder. Of this a dose of from 1 to 4 drams was given three or four times a day. Ludlam has recommended thymus gland in **dementia precox** (*q.v.*) on the basis of six successful cases.

BONE-MARROW ORGANO-THERAPY

The bone-marrow being the source of red corpuscles, its preparations have been tried in **pernicious anemia,** the **secondary anemias, chlorosis, malaria, leucocythemia, leukemia,** Hodgkin's **disease, rickets,** and other disorders of the osseous system. In all of these affections bone-marrow gave good results in some cases, while an equal number were in no way influenced. This obviously suggests that its indications coincide with certain phases or stages of the disease which have not as yet been determined. The average dose is 5 grains, after meals.

BRAIN AND NERVE SUBSTANCE ORGANOTHERAPY.

The belief, based on pure assumption, that brain and nerve substance possess or produce an internal secretion has never been sustained scientifically.

The clinical results, though quite discordant, particularly in the neuroses and psychoses in which these preparations have been tried, have shown a tendency to harmonize since the introduction by Sciallero of an oily extract. Page, who has obtained unusually good results in **neurasthenia** by means of injections of this extract, ascribes them to its antitoxic and antispasmodic effects. Wassermann and Takaki had previously shown that **tetanus** toxin was neutralized by contact with brain substance, and that when a fatal dose of tetanus toxin was injected with brain substance the fatal effects were prevented. The same observations were made in the case of **hydrophobia** by Babes; in **strychnine** and **morphine poisoning** by Widal and Nobécourt; in tetanus by Krokiewicz; in **epilepsy** by Lion, and also Kaplan, using Poehl's opocerebrin—in accord with Dana's experience several years earlier. Sciallero, who obtained encouraging results in **neurasthenia, hysteria, chorea, tic,** and **epilepsy,** used his oily extract "cephalopin" in doses varying from 1 to 5 c.c. (16 to 81 minims). No untoward effects were obtained.

Although it is very improbable that brain extracts injected into the tissues act as they do in the test-tube, it seems established that they act much as do the lecithins on the market, *i.e.,* by furnish-

ing phosphorus to the organism in an assimilable form, or as nucleoproteids in enhancing the immunizing process. Be this as it may, these substances seem to have produced effects which suggest that they should, not as yet, be set aside.

The writer used brain extract in dementia, various forms of insanity, dementia precox, and melancholia, and other mental disorders with material improvement in some. It has the sedative effect of the synthetic hypnotics, without their danger. The extract used at first was prepared from the brains of fetal calves and was prepared by boiling finely-divided brain tissue in alcohol and ether, and preparing an emulsion from the deposited material with normal saline solution. This extract is rich in cholesterin and in a substance that reduces Fehling's solution. W. Maule Smith (Brit. Med. Jour., Nov. 23, 1912).

The writer recalls the discovery of Howell that the so-called fibrin ferment is not really an enzyme, but a lipoid. As is well known, the fibrin ferment prepared from blood platelets has hemostatic properties and is at present extensively employed for this purpose. The author has prepared lipoid extracts by placing the brains of oxen in 3 equivalents of alcohol, shaking and decanting. The residue is gently strained through muslin and treated with threefold the amount of ether, shaken violently and filtered through cotton and paper. The dried filtrate is yellow, consists of Thudichum's kephalines and possesses strong hemostatic properties, through its power of accelerating coagulation. Hirschfelder (Berl. klin. Woch., Sept. 13, 1915).

A phosphatid extracted from brain tissue, variously known in the literature and trade as thromboplastin or kephalin, was tried by the writer at the Johns Hopkins Hospital clinics, to hasten coagulation and hemostasis after surgical operations upon the genito-urinary apparatus and espe-

cially prostatectomy. Packing was impregnated with kephalin and applied to the raw surfaces. There was practically no bleeding. The writer uses kephalin gauze and also coats catheters with it. H. L. Cecil (Jour. Amer. Med. Assoc., lxviii, 628, 1917).

MAMMARY GLAND ORGANO-THERAPY.

It is held by some that the mammary gland produces an internal secretion; but the evidence is so scant that it can hardly be taken into account.

Although mammary gland, introduced by Bell, of Glasgow, and in the United States by the late John H. Shober, has been used considerably, and has shown a marked stimulating action upon the uterus, the manner in which it produces this effect has remained obscure. An extract lowers somewhat, and but temporarily, the blood-pressure and the pulse. According to Shober, it diminishes the blood supplied to the uterus and thus controls hemorrhage, its action resembling that of ergot, though free of the unpleasant effects of the latter drug.

Mammary gland is prepared in the form of a tablet made of the desiccated gland of the sheep, each tablet representing 20 grains (1.32 Gm.) of the fresh gland. The dose is from 3 to 6 tablets daily.

The therapeutic application is restricted to the genital apparatus. In cases of uterine fibroids characterized by excessive menorrhagia and metrorrhagia the bleeding was found by Shober to be controlled in a few weeks and the periods become regular, normal, and free from pain. There is improvement in the patient's health and weight, and the tumors themselves diminish in size up to a certain point. In 43 cases treated by Fedoroff, complete cure occurred in one-third, *i.e.,*

33 per cent.; a reduction of volume in 43 per cent., and no result whatever in 14 per cent. The hemorrhages disappeared completely in 80.3 per cent. of the cases. According to Fedoroff, the best effects are obtained when the mammary extract is used hypodermically. The patient is thus placed in a better condition for any needed operation, and often the necessity for an operation is postponed. Where there is evidence of inflammatory or degenerative changes, or when serious pressure symptoms are not controlled after a reasonable trial, operation should not be delayed. The mammary gland is also useful in cases of **subinvolution** unassociated with malignancy or structural changes.

Mammary gland has also given good results, in the hands of Pozzi, in the uterine hemorrhages attending **metritis** of any kind. It decongests the organ and thus counteracts inflammation.

It has also been recommended to assist **uterine involution** and to enhance lactation in **agalactia**. Here, again, the results reported have been antagonistic. The dose is 5 grains (0.32 Gm.), repeated several times daily, preferably after meals.

> On the plea that the exciting cause of uterine fibroids and the accompanying hemorrhages is uterine hyperemia of ovarian origin, and that the antagonistic effect of the mammary principle is helpful because of its anti-ovarian influence, the writer found that in a large proportion of cases receiving mammary extract, the **menorrhagia** was effectively controlled and under its continued use large uterine fibroids often disappear even during the early reproductive period. The dose of mammary substance was 10 grains (0.65 Gm.), 3 times a day; in severe cases 1 Gm. (15 grains), 4 times a day may be given with extract of ergot 0.2 Gm. (3 grains) and extract of hydrastis

0.1 Gm. (1½ grains) with each dose and also, in some cases, X-ray to the ovaries every 3 weeks. W. A. Briggs (Endocrinology, Apr., 1917).

SPLEEN ORGANOTHERAPY.

This is based mainly on the prevailing opinion that the spleen destroys red corpuscles and creates new ones, and that it produces some sort of immunizing body, its leucocytes, as in lymphglands, being phagocytic.

Extracts of spleen have been tried in various disorders, including **exophthalmic goiter**, the **secondary anemias**, **pernicious anemia**, **chlorosis**, **lymphadenoma**, and **leucocythemia**, but the results have not been such as to warrant further trial. Bayle recommends it highly in **tuberculosis**.

> The writer administered fresh spleen substance with advantage in a number of cases of **anemia**. It reduced the proportion of nucleated reds in a remarkable manner and the clinical experiences were paralleled by similar findings in experiments upon animals. Brinchmann (Norsk Mag. f. Laegevidenskaben, Nov., 1916).

Pancot, Carpenter, and others claim to have obtained good results from splenic extract in the treatment of **malaria**. Lemansky found that it enhanced the action of quinine.

HEPATIC ORGANOTHERAPY.

Besides the functions carried on by the bile, which will be referred to below, the liver subserves several useful rôles. It is endowed with important antitoxic functions, all foodstuffs absorbed through the intestinal mucosa entering the organ through the portal system for this purpose. It supplies, out of the glycogen it forms, the blood and tissues the sugar they contain; it takes part in the metabolism of nitrogenous substances and forms urea. That

these many phases of usefulness should have suggested the use of hepatic substance is not surprising. Gilbert and Carnot found it useful in various conditions.

In **diabetes** liver extract was found to act with considerable energy; in some cases, however, the sugar was promptly diminished, even to *nil* occasionally, while in others it increased it. I have called attention to the fact that two forms of diabetes, the sthenic and asthenic, should be clearly distinguished from each other, the treatment of one form being pernicious in the other. It is in the asthenic form that hepatic extract will be found of value. Lereboullet has also observed beneficial effects in some cases.

One important feature of liver therapy is that, as emphasized by practical experience, the remedy causes diuresis in subjects who suffer from **hepatic insufficiency** in some form and particularly when it occurs in the course of **cirrhosis.** The diuresis is also accompanied by increased urea elimination.

In **alcoholic cirrhosis** it was also found of value by Gilbert and Carnot. The edema, jaundice, and hemorrhages were kept in abeyance in a case reported, returning whenever the use of liver extract was interrupted.

The coagulating action of liver on the blood, shown by Gilbert and Carnot, was carefully studied by Berthe. The patients on whom the observations were made were tuberculous, and had suffered repeatedly from **hemoptysis,** which had not responded to any ordinary treatment. In all cases the results were rapid. The method was also tried in cases of **epistaxis** and **metrorrhagia.** The method consisted in giving an extract of liver, about 3 drams (12 Gm.)

for a dose, in tepid soup. This amount will in many cases suffice, but can be repeated when necessary. It can also be administered per rectum in the same dose. One of the best and most suitable preparations is the *desiccated liver.* The *glycerin extract* is also efficacious. Should it not be possible to procure a ready-made extract, an *emulsion* of liver freshly prepared, and given in the form of an enema, seems to act perfectly well, 3 to 6 ounces (94 to 186 Gm.) being finely chopped up and then rubbed up with water, about 4½ ounces (140 Gm.) of liver being used. Fresh pigs' liver is one of the best sources of preparation.

Liver extract, now available on the market, has also been used with advantage in **chronic gastrointestinal intoxication,** the object being to check the growth of bacterial flora. Biliary acids, referred to below, are, however, preferable. A convenient way is to use the biliary extract in suppositories.

BILE, BILE-SALTS, AND BILIARY EXTRACTS.

The use of *bile* in therapeutics is based on a sounder basis than that of several of the foregoing agents, its excitomotor action on the intestine, now fully demonstrated, serving various useful purposes. It counteracts constipation due to intestinal atony, and thus prevents autointoxication of intestinal origin, which, in turn, produces cholangitis by allowing the return into the portal system of excretory products which should have escaped normally with the intestinal discharges. Again, bile, as shown by Pawlow, is a physiological auxiliary to the pancreatic juice, augmenting its activity threefold. As is well known also, bile, or gall, increases the solubility of cholesterin, thus preventing the formation of gall-

stones.   Bile is also endowed with anti-
toxic properties.

The therapeutic use of bile or bile
constituents is thus based on a solid
foundation.   They may be used as
stated above, in **constipation** and **putre-
faction** due to hepatic and intestinal
atony, **autointoxication** of intestinal
origin, in **cholangitis** and the resulting
jaundice, and also to prevent the for-
mation of **gall-stones.**   They have also
been used advantageously in **enteroco-
litis** in its membranous form.

Mucomembranous enterocolitis and
constipation being the result of insuffi-
ciency of the biliary secretion, their
treatment becomes simple.   The general
indications are: (1) reduction to a
minimum of the quantity of toxic and
putrefactive products in the intestine by
an appropriate diet; (2) shortening of
the period of transit of food through
the alimentary canal and prevention of
the coagulation of mucus by the use of
a cholagogue, the best of which is bile
itself.   The writer uses an extract de-
void of putrescible nucleoalbumins,
which he has termed *antimucose*, avail-
able in 0.20-Gm. (3.1 grains) dragées;
suppositories, and ampules of 50 c.c.
(1.7 fluidounces) in which the biliary
substances, dissolved in water, occur in
the concentration of normal bile.   H.

Nepper (Monthly Cyclopedia and Med.
Bull., Jan., 1912).

The writer found bile a powerfully
cytolytic agent, owing to the coen-
zyme or activating action of its con-
stituents on the autolytic enzymes or
processes.   Whole bile was found
more powerful though less penetrat-
ing than corresponding concentra-
tions of either of the bile salts.
Tatum (Jour. of Biol. Chemistry,
Oct., 1916).

Although cholic acid is the most
active of the bile-salts, salts of glyco-
cholic or taurocholic acid are preferred.
They possess all the therapeutic prop-
erties of oxgall.   The **sodium glyco-
cholate** or **taurocholate** can be con-
veniently used in $\frac{1}{2}$- to 3- grain
(0.032 to 0.19 Gm.) doses three times
a day.   Or, the **extract of bile** may be
given in 5- to 15- grain (0.32 to 1.0
Gm.) doses after meals, with a
draught of water.   Bile may also be
injected into the rectum to cause its
evacuation.   This is especially valu-
able in **paralytic ileus, postoperative**
and **peritonitic atony,** or **paresis** of the
intestine from any cause.

C. E. de M. Sajous
Philadelphia.